A STUDY ON THE ASSOCIATION OF MEAN PLATELET VOLUME WITH ISCHAEMIC STROKE AND ITS CORRELATION WITH STROKE SUBTYPES

Dissertation submitted in

Partial fulfilment of the regulations required for the award of

M.D. GENERAL MEDICINE

BRANCH I

THE TAMILNADU

DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

APRIL 2015

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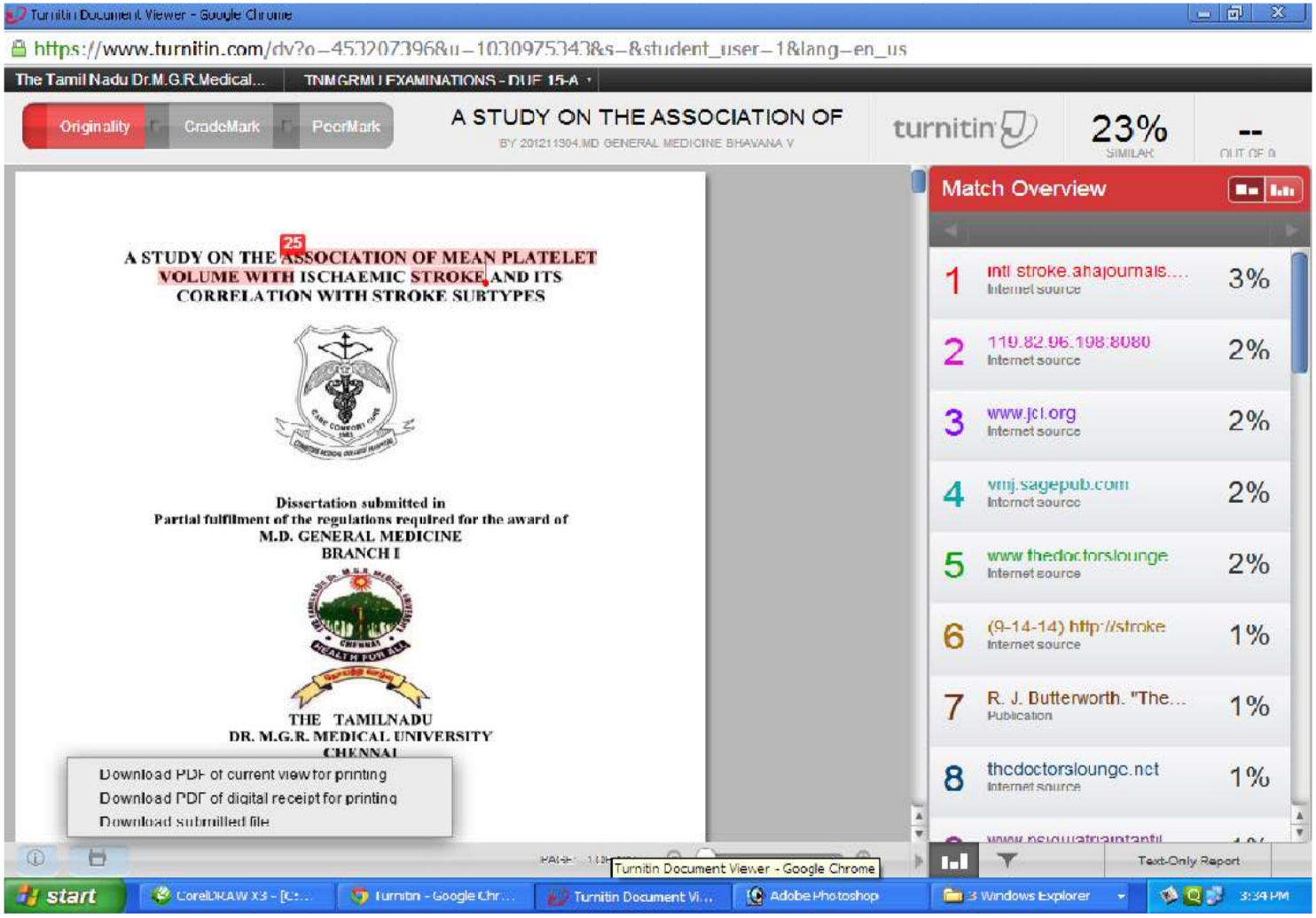
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TABLE OF CONTENTS

S.NO	TITLE	PAGE NO
1	INTRODUCTION	1
2	AIMS AND OBJECTIVES	4
3	REVIEW OF LITERATURE	5
4	MATERIALS AND METHODS	48
5	OBSERVATIONS AND RESULTS	71
6	DISCUSSION	87
7	SUMMARY	96
8	CONCLUSION	100
9	BIBLIOGRAPHY	101
10	ANNEXURES	
	PROFORMA	109
	CONSENT FORM	114
	MASTER CHART	118
	KEY TO MASTER CHART	129

LIST OF TABLES

SL NO	TITLE OF TABLE	PAGE NO
1	Risk factors of stroke	20
2	Structural zones of platelet	28
3	Contents of the different granules of platelets	30
4	Stroke log and reasons for exclusion	71
5	Age distribution	73
6	Gender distribution	75
7	Risk factor profile	76
8	Clinical profile	77
9	The Oxfordshire community stroke project classification of stroke	79
10	Stroke clinical severity score	80
11	Comparison of platelet counts in cases and controls	81
12	Comparison of MPV in cases and controls	82
13	Stroke subtypes and MPV	84
14	Correlation between platelet count and stroke subtype	85
15	Correlation between stroke severity and MPV	86
16	Comparison of demographic data of current study with western literature	88
17	Comparison of risk factor profile of current study with western literature	89
18	Comparison of drug history of patients in current study with western literature	90
19	Comparison of platelet parameters of current study with western literature	91

LIST OF CHARTS

SL NO	TITLE OF THE CHART	PAGE NO
1	Stroke log and reasons for exclusion	72
2	Age distribution	74
3	Gender distribution	75
4	Risk factor profile	77
5	Clinical profile	78
6	Stroke subtypes	80
7	Stroke clinical severity score	81
8	Comparison of platelet counts in cases and controls	82
9	Comparison of MPV in cases and controls	83
10	Stroke subtypes and MPV(EDTA)	84
11	Stroke subtypes and MPV(citrate)	85
12	Correlation between platelet count and stroke subtype	86

LIST OF FIGURES

SL NO	TITLE OF FIGURES	PAGE NO
1	Anterior circulation	7
2	Arterial supply to brain	10
3	Circle of Willis	11
4	Cortical vascular territories	12
5	Anatomy of proplatelets	23
6	Microscopic appearance of platelets on Leishman stained smear	24
7	Subcellular organization of resting platelet	27
8	Structural zones of platelet	28
9	Formation of a haemostatic platelet plug	34
10	Platelet formation	40
11	Principle behind automated haematology analyser	53

ABBREVIATIONS

ACA - anterior communicating artery

ACE- angiotensin converting enzyme

ADP-adenosine diphosphate

ATP- adenosine triphosphate

ATP-3 –adult treatment panel -3

b-TG- b-thromboglobulin

CCA- common carotid artery

CT-computed tomography

DNA- deoxy ribonucleic acid

ECA-external carotid artery

EDTA-ethylene diamine tetra acetic acid

fL-femtolitre

ICA- internal carotid artery

LACS- lacunar syndrome

MCA-middle cerebral artery

MK- megakaryocyte

MPHA- megakaryocyte platelet haemostatic axis

MPV- mean platelet volume

NIHSS- national institutes of health stroke scale

OCSP- Oxfordshire community stroke project

PACS- partial anterior circulation syndrome

PCA- posterior cerebral artery

PCT- platelet count

PDW- platelet distribution width

PoCA- posterior communicating artery

POCS- posterior circulation syndrome

PROGRESS- perindopril protection against recurrent stroke study

SCCS- surface connected canalicular system

SOP- standard operating procedure

TACS- total anterior circulation syndrome

TIA- transient ischaemic attack

vWF- von Willebrand factor

ABSTRACT

Background and Objectives

Stroke is one of the most common neurological disorders. Ischaemic stroke occurs due to thrombus occluding a stenosed atherosclerotic blood vessel. Platelets have a crucial role in the pathophysiology of atherothrombosis. Ischaemic Cerebrovascular disease (ischaemic stroke) is one of the leading public health problem. From the late 1990s, there has been an increase in survival after stroke. So it has become a very common cause of suffering and one of the leading cause of long-term disability.

Large platelets are more reactive, produce more prothrombotic factors and aggregate more easily. So the detection of large platelets in patients with ischaemic stroke support the idea that platelet volume influences thrombotic large vessel occlusion. There are very few documented studies in India comparing the association of mean platelet volume with ischaemic stroke. So I intend to make an attempt to find out the association between mean platelet volume and ischaemic stroke. Objectives of the study was to find out whether a significant association exist between the occurrence of ischaemic stroke and mean platelet volume as well as to find out whether a significant association exist between stroke subtype and mean platelet volume.

Methods:

The study was a prospective case control study conducted at Coimbatore Medical College and data was collected over a period of six months from December 2013 to may 2014. The study was conducted amongst100 patients diagnosed with acute ischemic stroke and who presented to the hospital within 48 hours of onset of symptoms. Hundred controls were also selected. Controls were matched for age, sex,known risk factors including hypertension, diabetes, dyslipidemia, smoking,and alcoholism.

Each case was assessed and severity of stroke assessed using the NIHSS. Blood sample was collected for measuring mean platelet volume, peripheral smear and platelet count.

Results

The main parameter studied was MPV. MPV has got a statistically significant correlation with ischaemic stroke with a p value less than 0.001. The average MPV in cases was 8.35±0.98 (EDTA) and 7.93±0.99 (citrate). The average MPV in controls being 7.81±0.79 (EDTA) and 7.30±0.74 (citrate). Therefore, the study shows an elevated MPV in the acute phase of ischaemic stroke. This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume. This study also showed no statistically significant correlation between mean platelet volume and stroke subtypes.

Key words: Ischaemic stroke; stroke outcome;mean platelet volume; platelet

INTRODUCTION

Stroke is one of the most common neurological disorders. Ischaemic stroke occurs due to thrombus occluding a stenosed atherosclerotic blood vessel. Platelets have a crucial role in the pathophysiology of atherothrombosis. Ischaemic Cerebrovascular disease (ischaemic stroke) is one of the leading public health problem. Every 53 seconds, one individual in the United States gets a stroke. Every year, around 750,000 Americans have a first or recurrent ischaemic stroke. Stroke incidence is much more common in other countries. Rates are especially high in Asia and Eastern Europe. Occurrence rates of stroke differ considerably among different regions; for example, the incidence of stroke is decreasing in Western Europe and North America while it is on the rise in Eastern Europe. Definitive data about stroke from many developing and underdeveloped countries are unavailable.But stroke is likely to be a major health problem in these nations. Increase in life expectancy of individuals in developing countries has made stroke an important worldwide problem.[65,66] In India, community surveys show a prevalence rate for hemiplegia in the range of 200 per 1,00,000 persons. Stroke accounts for nearly 1.5 percent of all urban hospital admission, 4.5% of all medical and around 20% of all neurological cases.[67] Stroke is next only to heart disease as a leading cause of death worldwide.

From the late 1990s, there has been an increase in survival after stroke. So it has become a very common cause of suffering and one of the leading cause of long-term disability. A stroke often precludes patients' capacities to return to work or to regain their role in family. Thus stroke is a family illness. Disability may require a spouse or other relative to assume a new role or become a full-time care giver. Stroke is second only to dementia as a neurological disorder leading to long term institutionalized care. Recurrent stroke produces dementia, and its effects exacerbate cognitive impairments from degenerative dementias, such as Alzheimer's disease.[65]

Due to the high incidence of stroke and the high costs expended for each individual patient, it accounts for a sizeable amount of the health care costs. Thus, stroke and its sequelae are important issues for health care planners. Because the costs of treatment and the economic consequences of lost productivity are so great, prevention of stroke will be a very cost effective strategy.[65]

Ischaemic cerebrovascular disease encompasses a broad spectrum of clinical events based on the type and duration of the neurological symptoms, the area of brain affected, the involved artery, and the presumed cause. This classification is important in establishing a patient's prognosis and making decisions about evaluation and treatment.

Although the term cerebrovascular accident (CVA) is used widely by physicians and other health care professionals, it is an appalling pseudoscientific characterization of stroke that substitutes labeling for understanding. The term should be abandoned because many strokes are not accidents, but preventable catastrophes.

A stroke is rapidly developing clinical symptoms and / or signs of focal, and at times global loss of brain function with symptoms lasting more than 24 hrs or leading to death, with no apparent cause other than that of vascular origin.[68]

Thus, the definition of stroke is clinical and laboratory studies including brain imaging are used to support the diagnosis. The clinical manifestations of stroke are highly variable because of the complex anatomy of the brain and its vasculature.[69]

Large platelets are more reactive, produce more prothrombotic factors and aggregate more easily. So the detection of large platelets in patients with ischaemic stroke support the idea that platelet volume influences thrombotic large vessel occlusion. There are very few documented studies in India comparing the association of mean platelet volume with ischaemic stroke. So I intend to make an attempt to find out the association between mean platelet volume and ischaemic stroke.

OBJECTIVES

1. 1.To find out whether a significant association exist between the occurrence of ischaemic stroke and mean platelet volume.

2. To find out whether a significant association exist between stroke subtype and mean platelet volume.

3. To find out the association between stroke severity and mean platelet volume.

3.1 STROKE

3.1.1 HISTORY

The father of medicine, Hippocrates, described stroke as a sudde onset paralysis around 2400 years ago. Cerebrovascular disease is historically more ancient than heart disease. In ancient era, stroke was known as apoplexy [15].Apoplexy was a recognized clinical syndrome and cause of death before the time of Hippocrates. Johan Jakob Weefer a Swiss Physician (1620-1695) seems to have been the first to suggest that apoplexy was caused by blood vessels of the brain.[15] Discrimination between cerebral hemorrhage and cerebral infarction was made by Morgagni (1682-1771) of Padua. William Sen House Kirles (1852) was the first to give description of cerebral embolism. Panam first proposed that debris from atherosclerotic plaques can cause emboli. This view was accepted and the yellow softening, described by Ring Fleisch in 1873 was agreed to be due to preceeding obstruction of the supplying artery, usually by a clot and cerebral thrombosis was established as an important cause of stroke.

Loman and Myerson in 1936 introduced coronary angiography. Godfrey Hounsefield in 1972 invented CT scan and has revolutionized the diagnosis and treatment of stroke.[70]

3.1.2 EPIDEMIOLOGY

3.1.2a: INCIDENCE AND PREVALENCE

Occurrence of cerebrovascular disease increases with age.They are amongst major causes of disability.As the elderly population increases ,there will be an increase in the number of strokes.It is expected that there would be a doubling of deaths in the United States by the year 2030.[10]

3.1.2b:INDIAN SCENARIO

The stroke prevalence in India was found to be 203 per 100,000 in above 20 years of age population .This shows that there would be around one million cases in India . Ratio between males and females is around 1.7.The prevalence of stroke in population below 40 years is around 12%.It is estimated that around 1.2% of total deaths in India is due to strokes.[13]

3.1.3 ANATOMY

BLOOD SUPPLY TO THE BRAIN

The brain constitutes 2 percent of total body weight. But it receives almost 20 percent of the cardiac output at rest. It also consumes about 20 percent of total inspired oxygen. The rich blood supply is by the 2 internal carotid and 2 vertebral arteries. They anastomose at base of brain forming the

circle of Willis. Carotid arteries supply the anterior parts of the brain. Vertebrobasilar arterial system supplies the posterior portions of the brain.[69]

Internal carotid artery (ICA) :begins as carotid sinus at the bifurcation of common carotid artery (CCA) ,at the level of thyroid cartilage. It courses up the neck, without giving any branches, to the base of skull. It course through the foramen lacerum to enter the carotid canal of petrous bone. It then runs through the cavernous sinus in an S-shaped curve (the carotid siphon), pierces the dura, and exists just medial to the anterior clinoid process.It then bifurcates into anterior cerebral and large middle cerebral artery.[69]

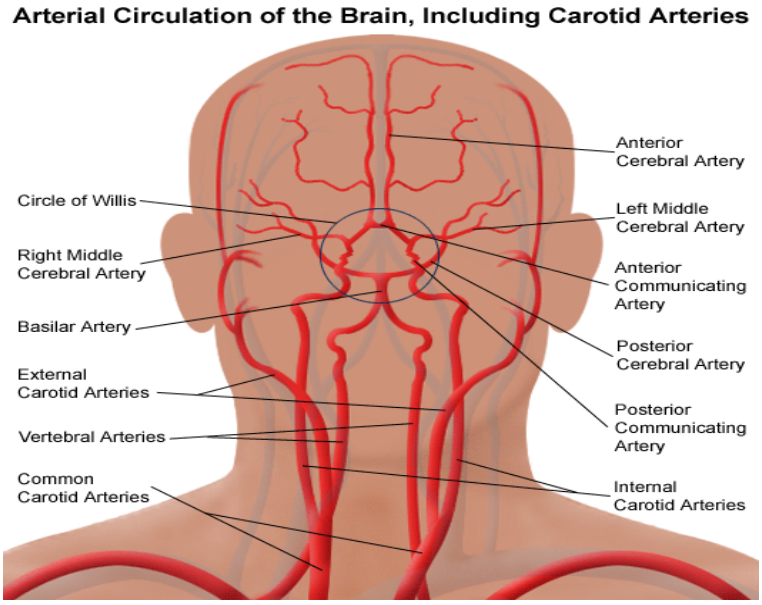


Fig.1 : Anterior circulation

External carotid artery (ECA) :starts at the CCA bifurcation. Branches supply the jaw, face, scalp, neck, as well as meninges (superficial temporal, facial, occipital arteries, etc).[69]

ICA gives off its first major branch, the **ophthalmic artery** and arises in the cavernous sinus. It courses through optic foramen to supply eye and other parts in the orbit.[69]

The posterior communicating artery (PoCA) is the next to arise from the ICA. It courses backwards to join first part of the posterior cerebral artery, thereby contributing to the circle of Willis. Small branches also supply adjacent optic chiasm, hypothalamus, and midbrain.[69]

The **anterior choroidal artery** arises from the last section of ICA, just beyond the PoCA origin.It supplies the optic tract, internal capsule, basal ganglia, the medial part of temporal lobe, thalamus, lateral geniculate body, proximal optic radiation, and midbrain. It may arise from proximal middle cerebral artery or PoCA. Minor twiglets from distal ICA contribute blood to the pituitary gland, optic chiasm, and the meninges.[69]

Anterior cerebral artery (ACA): enter the interhemispheric fissure, anastomoses with its counterpart on the opposite side through the anterior communicating artery (ACoA), curves up around genu of the corpus callosum, and supplies anterior and medial parts of cerebral hemisphere. Few small

branches supply parts of the optic nerve ,optic chiasm, hypothalamus, anterior basal ganglia, and internal capsule.[69]

Middle cerebral artery (MCA): enter Sylvian fissure , gives off 2-4 branches which supply lateral parts of cerebral hemisphere. Main trunk gives off medial and lateral groups of tiny lenticulostriate arteries and arterioles, which penetrate base of the brain and supply basal ganglia and internal capsule. A few of these small penetrating vessels extend up to the white matter of corona radiata.[69]

Vertebral artery: arises from proximal part of subcalvian artery .It ascends through transverse foramina of sixth to second cervical vertebrae, giving off many small muscular branches during its course. It then courses posteriorly around articular process of atlas vertebra to enter skull through foramen magnum. It joins the opposite vertebral artery on ventral surface of brainstem at pontomedullary junction to form basilar artery. Branches to the meninges are given off at the foramen magnum. The vertebral artery gives off the anterior and posterior spinal arteries, posterior inferior cerebellar artery (which supply inferior vermis and posterior as well as inferior surfaces of cerebellar hemispheres, and brainstem), and small penetrating arteries tosupply medulla.[69]

Basilar artery: ascends ventral to the pons till the pontomidbrain junction in the interpeduncular cistern. Here it divides into two posterior cerebral arteries. Several small branches penetrate the brainstem and thecerebellum. The basilar artery gives off anterior inferior cerebrellar artery (to cerebellum, brainstem, inner ear) and superior cerebellar artery (to brainstem, superior half of cerebellar hemisphere, vermis, and the dentate nucleus).[69]

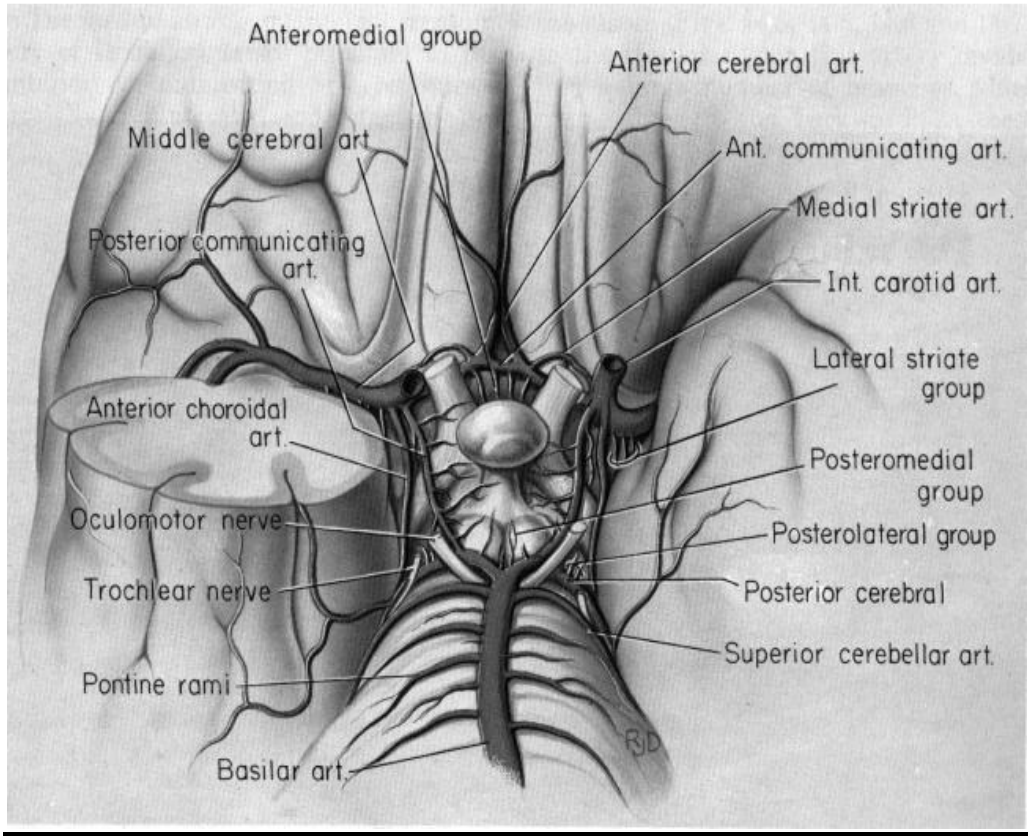


Fig:2 Arterial supply to brain

Posterior cerebral artery (PCA) :encircles midbrain close to oculomotor nerve at the level of the tentorium .It supplies inferior part of temporal lobe, and the occipital lobe. Several perforating arteries arise from

proximal portion of PCA to supply the midbrain, thalamus, hypothalamus, and the geniculate bodies.

In 15 percent people, the PCA is a direct continuation of the PoCA. In this situation, its main blood supply comes from the ICA rather than basilar artery.[69]

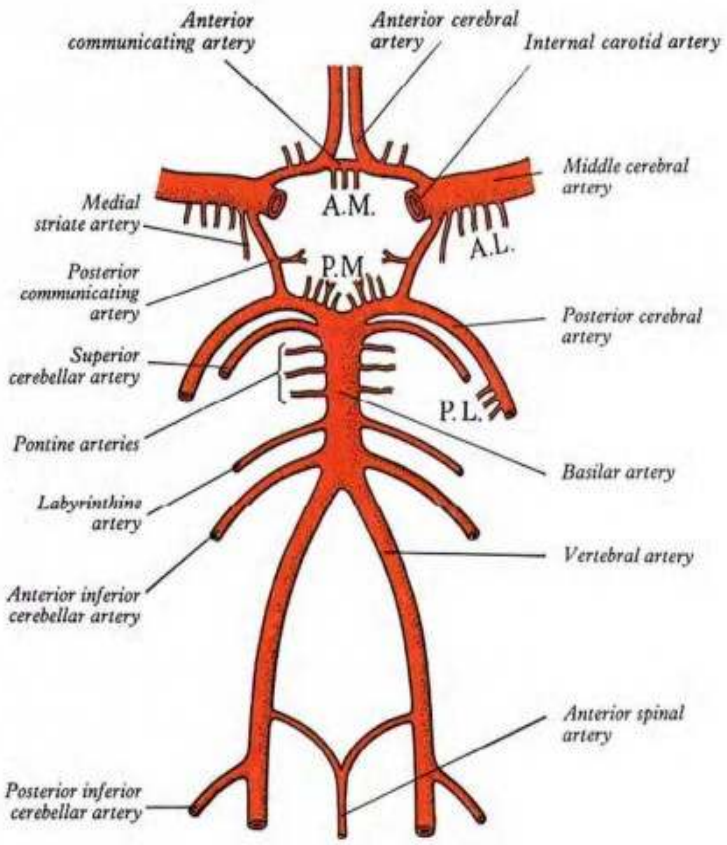
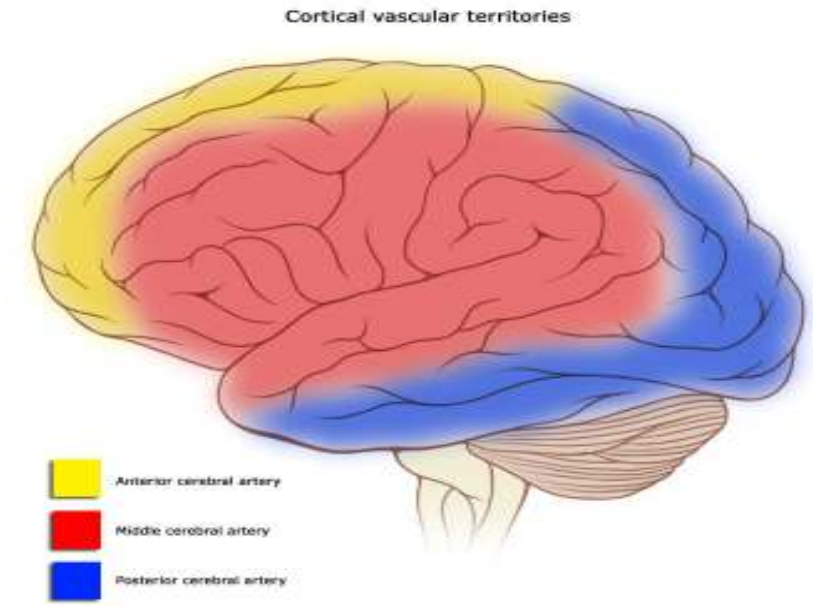


Fig:3 Circle of Willis

Fig4:Cortical vascular territories



3.1.4 PATHOPHYSIOLOGY

A fall in cerebral blood flow to almost nil causes death of brain tissue within four to ten minutes. A rate of blood flow less than 16 ml/100g tissue per minute cause infarction of brain tissue in about one hour .A flow rate less than 20ml per 100g of brain tissue per minute cause ischaemia,but no infarction, unless persistent for hours to days.

TIA occurs if blood flow is reestablished before significant cell death. The tissue which surround the core area of infarction is ischaemic but this area is reversibly dysfunctional .This area is called the ischaemic penumbra. The ischaemic penumbra undergo infarctionif there is no change in blood flow.

Revascularization procedures are based on this and they aim at preserving ischaemic penumbra.[10]

There are two different pathways for the occurrence of cerebral infarction.First is the necrotic pathway, in which cytoskeleton within the cells breakdown rapidly due to energy failure .Second is the apoptotic pathway in which cells are programmed to die.

Ischaemia produces glucose deficiency in neurons. This result in necrosis leading to reduced production of ATP by mitochondria.ATP deficiency result in malfunctioning of membrane ion pumps, which in turn lead to neuronal depolarization. Hence, the intracellular calcium rises as well as there is release of glutamate from the synaptic terminals. Excess of extracellular glutamic acid in turn activates postsynaptic glutamate receptors .Receptor activation further leads to an increase in the neuronal calcium influx. All these mechanisms lead to neurotoxicity.

Destruction of membrane lipids and mitochondrial dysfunction favour the formation of free radicals. Free radicals induce catalytic damage of membranes. Ischaemic penumbra, having lesser degree of ischaemia ,favours apoptotic cell death after few days to weeks .[10]

3.1.5 ETIOLOGY

(A)COMMON CAUSES

(a)Thrombosis

- ❖ Lacunar stroke
- ❖ Thrombosis of large vessels.
- ❖ Severe dehydration

(b)Embolic Occlusion

- ❖ Artery to artery
  - Aortic arch
  - Carotid bifurcation
  - Dissection of artery
- ❖ Cardioembolism
  - Intra mural thrombus
  - Atrial fibrillation
  - Myocardial infarction
  - Dilated cardiomyopathy
  - Valvular lesions
  - Infective endocarditis
  - Mechanical cardiac valves
- ❖ Paradoxical embolus
  - Atrial septal defect/ASD
  - Patent foramen ovale

B.UNCOMMON /RARE CAUSES

(a)HYPERCOAGULABLE STATES

- Deficiency of protein C/ ProteinS/ Antithrombin III
- Antiphospholipid antibody syndrome
- Factor V Leiden mutation
- Prothrombin gene G20210 mutation
- Systemic lupus erythematosus
- Systemic malignancy
- Sickle cell anaemia
- Homocysteinemia
- β Thalassemia
- Polycythemia vera
- Thrombotic thrombocytopenic purpura/TTP
- Disseminated intravascular coagulation/DIC
- Nephrotic syndrome
- Inflammatory bowel disease
- Oral contraceptives

(b) Venous sinus thrombosis

(c) Fibromuscular dysplasia

(d) Vasculitis

- Systemic vasculitis (Polyarteritis nodosa/PAN , Wegner's granulomatosis, Takayasu's andgiant cell arteritis)

- Primary CNS vasculitis
- Meningitis (tuberculosis, fungal, bacterial, zoster,syphilis)

(e)Cardiac causes

- Calcified mitral valve
- Atrial myxoma or other Intracardiac tumour
- Libman sacks endocarditis
- Marantic endocarditis

(f)Subarachnoid haemorrhage leading to vasospasm

(g) Drugs : including Cocaine, amphetamine

(h) Pregnancy-Eclampsia

(i) Moyamoya disease

3.1.6 DEFINITIONS

TIA : when all neurological signs and symptoms resolve within a period of 24 hours irrespective of the presence or absence of imaging evidence of new permanent brain injury.[10,12]

STROKE: is said to have occurred if the neurological signs and symptoms last for more than 24 hours.[10,12]

3.1. 7CLASSIFICATION

The Oxfordshire Community Stroke Project [12] classifies stroke into 4 syndromes based upon clinical features. Once the stroke lesion is complete and before resolution of any of the signs,the positive and negative predictive values against brain imaging is good.

1) LACUNAR SYNDROMES (LACS)

- Pure motor weakness
- Pure sensory deficit of one half of body
- Sensory motor hemiparesis
- Ataxic hemiparesis (dysarthria clumsy hand syndrome or ipsilateral ataxia with crural hemiparesis
- There should not be any visual field defects
- There should not be any new disturbance of higher cortical or brainstem function.
- Atleast 2 of the three areas (face,arm,leg) must be involved fully.

2) POSTERIOR CIRCULATION SYNDROME (POCS)

Any one of the following should be present-

- Cranial nerve involvement
- motor or sensory deficit-unilateral or bilateral
- conjugate eye movement disorder
- Homonymous hemianopia
- Cerebellar involvement
- Cortical blindness

3) TOTAL ANTERIOR CIRCULATION SYNDROME (TACS)

- ❖ Hemiplegia and homonymous hemianopia opposite to the side of Lesion
- ❖ aphasia or visuospatial disturbance
- ❖ Sensory deficit on contralateral side of lesion

4) PARTIAL ANTERIOR CIRCULATION SYNDROME /PACS

- ❖ One or more of unilateral motor or sensory deficit or aphasia or visuospatial neglect (with or without homonymous hemianopia)
- ❖ Motor or sensory deficit less extensive compared tothat in lacunar syndromes (eg: hand alone)

3.1.7: TABLE 1: RISK FACTORS OF STROKE

Risk factors	Relative Risk	Relative risk Reduction [with Treatment]	Number needed to treat	
			Primary prevention	Secondary prevention
Hypertension	2-5	38%	100-300	50-100
Atrial fibrillation	1.8-2.9	68% warfarin and 21% Aspirin	20-83	13
Diabetes mellitus	1.8-6	No proven benefit	_	_
Smoking	1.8	50% at 1 year, baseline risk at 5 years after cessation	_	_
Hyperlipidemia	1.8-2.6	16-30%	560	230
Asymptomatic carotid Stenosis	2.0	53%	85	N/A
Symptomatic carotid stenosis(70-99%)	_	65% at 2 years	N/A	12
Symptomatic carotid stenosis(50-69%)	_	29% at 5 years	N/A	77

3.2 PLATELETS

Platelets are small in size and are anucleate. They play a central role in haemostasis as well as thrombosis[16]. Addison described platelets as "extremely minute" granules. The term 'platelet' was coined by Bizzozero. He described their adhesive property as "increased stickiness" on damage of vessel wall".

Platelets form from the cytoplasm of megakaryocytes. They are discoid in shape and have an average size of 2μm. Younger platelets are functionally more able. Each megakaryocyte forms around 10^3 platelets and 10^{11} platelets are replenished daily[17].

3.2.1 PLATELET FORMATION

3.2.1. a. Megakaryocyte Development

Megakaryocytes are myeloid cells (<1% of myeloid cells) present mainly in the bone marrow. They are also present in the lung and peripheral blood. During development, megakaryopoiesis occurs initially within the foetal liver and yolk sac. Megakaryocytes arise from pluripotent stem cells that develop into 2 types of precursors: burst forming cells as well as colony forming cells. Both precursors express CD34 antigen[64]. Thrombopoietin(TPO) is primary regulator of thrombopoiesis,which is presently only known cytokine required for megakaryocytes to maintain a constant platelet mass. TPO acts in conjunction with other factors like IL-3, IL-6, and IL-11,which are not a necessity for megakaryocyte maturation[64].

3.2.1b THE FLOW MODEL OF PLATELET FORMATION

The mechanism of in platelet synthesis is still not known clearly. Recent research and evidence favours a modified flow model. In this model, platelets are thought to assemble along intermediate pseudopodial extensions . These

extensions are known as proplatelets. These proplatelets form as a result of outflow and evagination of internal membrane system of the mature megakaryocyte. Wright introduced the concept that platelets arise from megakaryocyte extensions in 1906. He described this as the detachment of platelets from megakaryocyte pseudopods[64]. Recent studies have supported this concept of platelet fragmentation from the ends of megakaryocyte extensions[64].

The formation of platelets from megakaryocytes involve an elaborate procedure, converting the cytoplasm into 100- to 500-µm long branched proplatelets upon which the individual platelets develop. The process of proplatelet and platelet formation commences at a single site on the megakaryocyte where one or more broad pseudopodia form. The pseudopodial extension elongate over a period of four to ten hours. They taper into proplatelets with an average diameter of 2 to4µm[64]. Proplatelets have multiple bulges or swellings , each of which is similar in size to a platelet.This gives the appearance of beads connected by thin cytoplasmic threads. The generation of proplatelets continue to spread in a wave like manner throughout the cell until the whole of the megakaryocyte cytoplasm is transformed into an extensive network of interconnected proplatelets. The nucleus of megakaryocyte shrinks into a central mass with scanty cytoplasm and it is finally extruded. swellings develop at the proplatelet ends, which are the main sites of platelet assembly and release, unlike swelling along the proplatelet shaft[64].

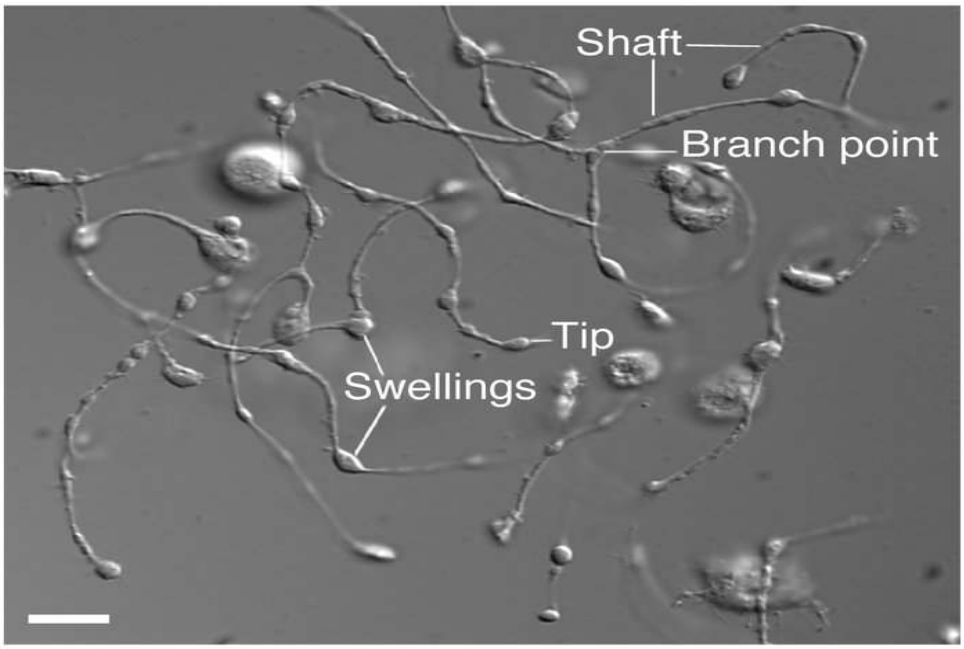


Figure5: anatomy of proplatelet- differential interference contrast image of proplatelets showing features of proplatelets like tip, shaft, swellings, and branch point[64] - mouse megakaryocyte

3.2.2 PLATELET LIFE SPAN

The average lifespan of platelets is 7-10 days. They are removed from circulation via two mechanisms. One is by senescence in which senescent cells are destroyed mainly by splenic macrophages. The larger blood flow of liver permits a faster removal of the damaged platelets by hepatic macrophages[17]. Aging platelets have lesser amounts of sialic acid and more of surface IgG[18]. The other way of removal is random removal in endothelial supportive functions of a fixed fraction of platelets amounting to almost 7.1×10^9/l per day.

3.2.3 LIGHT MICROSCOPY

Under the light microscope, smears stained with Wright stain under the light microscope reveals that platelets are small, anucleate with few reddish granules. They exhibit considerable variation in size as well as shape. They measure 2μm in diameter[19,20].

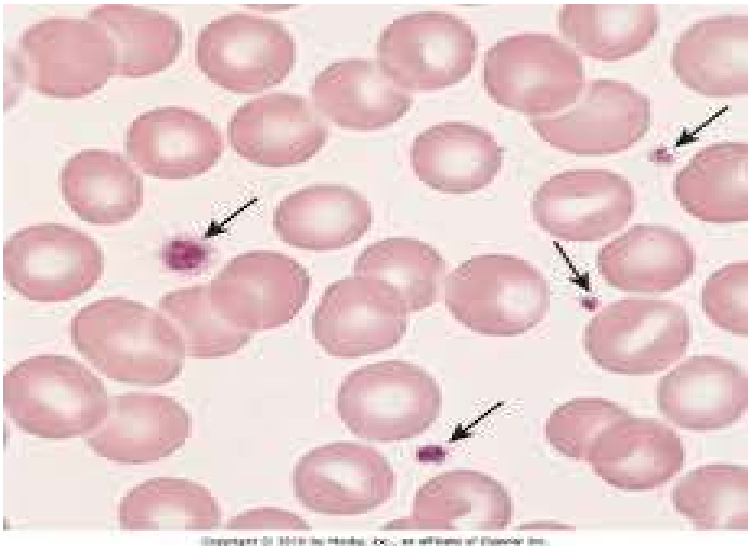


Figure6: microscopic appearance of platelet in Leishman stained smear (x1000)

3.2.4 ELECTRON MICROSCOPE ANDSUBCELLULAR FEATURES

Platelets have two forms- resting and activated. The resting state has baseline metabolism. The activated state is as a result of agonist stimulation (i.e thrombin). Platelets have a change in structure during the transition from resting to activated state. Transmission electron microscopy reveals major information regarding platelet anatomy.

3.2.5 PLATELET SURFACE

Plasma membrane: It is 20nm thick and trilaminar[22]. Though the overall appearance is similar to that of other blood cells[23],it hasa much more complex composition and function. It incorporates a variety of glycoproteins along with lipids onto phospholipid bilayer and it coordinates a variety of extra and intra-platelet events which include permeability,adhesion, activation and aggregation[24].

Glycocalyx: It is a fuzzy layer composed of lipids, proteins, and sugars. It is about 15to 20 nm in thickness. It coats outside of plasma membrane. It interacts with the plasma as well as the cellular components of blood and blood vessels. The layer acts as a transfer point for plasma proteins like fibrinogen, as they are

taken up into secretory granules by endocytosis[25,26].

It is rich in mucopolysaccharides, glycoproteins, glycolipids, ,and plasma proteins that are absorbed[27,28]. This gives a net negative surface charge, mainly because of te prescence of sialic acid residues on proteins such as gpIb[29]. A net negative charge prevents binding of circulating platelets to each other and also to the vessel wall[30].

3.2.6 THE MEMBRANOUS SYSTEMS OF PLATELET

Platelets have properties similar to that of muscle cells such as high content of actin and contractile response on activation. There are two membranous systems in platelets. One is surface connected canalicular system [SCCS] which resemble transverse tubules. The other is dense tubular system which resemble sarcotubules. They have muscle like properties[23]

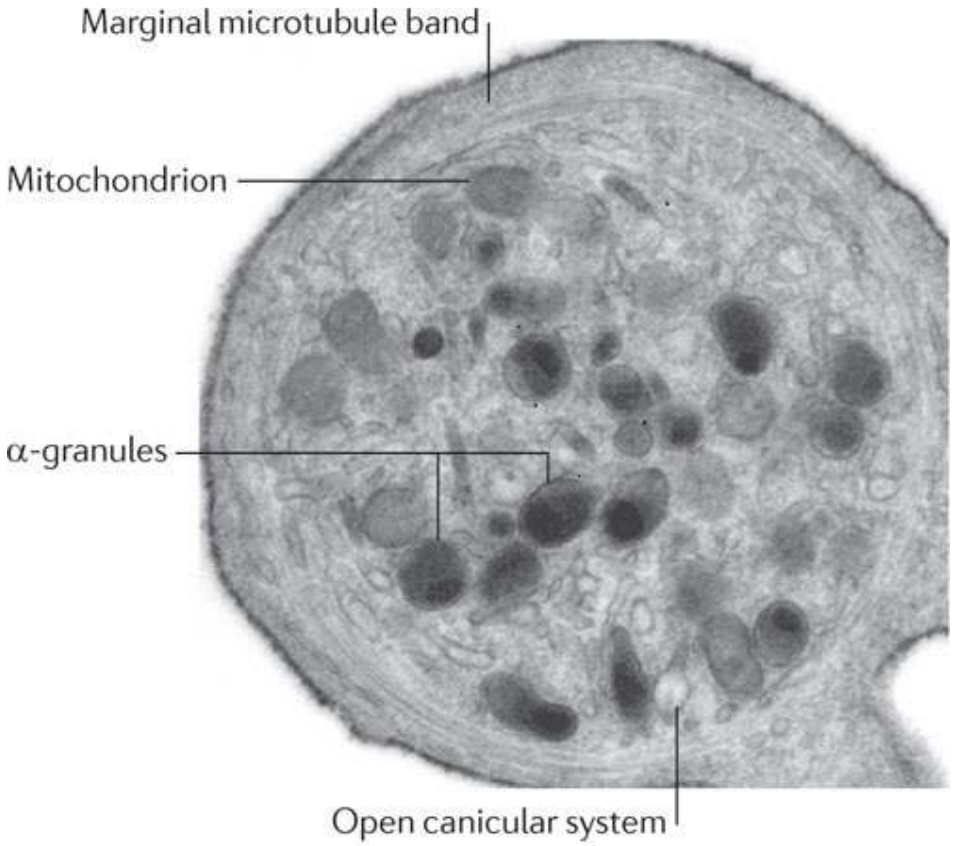


Fig 7:Subcellular organization of resting platelet- electron microscopy view. The marginal microtubule band encircling cytoplasm of platelet to maintain discoid shapeof platelet. α-granule forms the majority of storage granules. Dense granules, mitochondria, peroxisomes and lysosomes are interspersed[65].

Three main structural zones

1. Peripheral
2. Membranous
3. Organelle

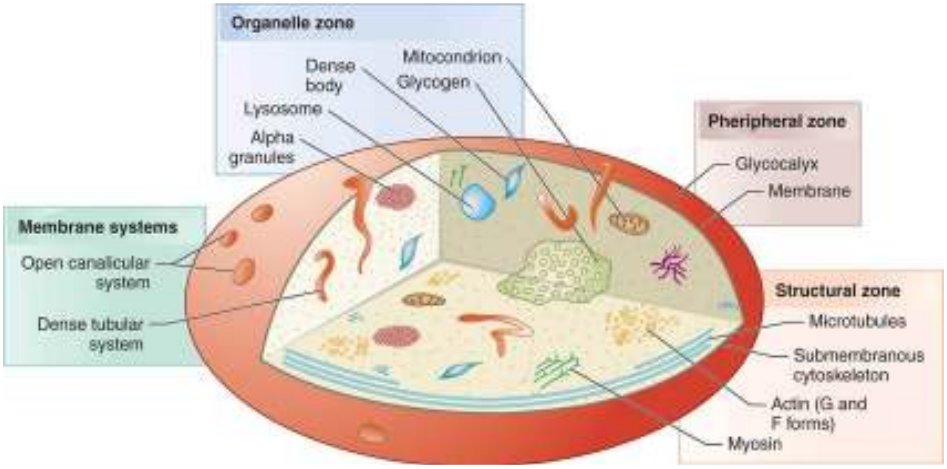


Fig 8: structural zones of platelet

Table 2: structural zones of platelet

Peripheral Zone	Membranous Zone	Organelle Zone
> function is adhesion and aggregation, responsible for cell's negative charge > Glycocalyx *(exterior coat)* - consists of coagulation factors *(I, II, VII, IX, X)* - Receptors (Glycoproteins Ib/IX, IIb/IIIa)) > Membrane - phospholipids and proteins embedded within it - the location of pumps, channels, receptors, enzymes, and structural proteins - Responsible for the release of fatty acid derivatives	function is structure and support > OCS (Open Canalicular System) - responsible for the secretion of granule contents > DTS (Dense Tubular System) - responsible for the storage of calcium - major site of prostaglandin and thromboxane synthesis	function is secretion and storage > Mitochondria > Glycogen > Granules, which serve as storage sites for proteins and other substances necessary for platelet function

3.2.7 PLATELET CYTOSKELETON

The cytoskeleton of platelet is composed of cytoplasmic framework of monomers, tubules and filaments[32]. The function of cytoskeleton include production of shape change, formation of extracellular extensions, collection and extrusion of secretory granules. They also affect surface activity. There are three different structures in the cytoskeleton which are responsible for the above functions. First is the membrane skeleton buttressing the inner side of plasma membrane. Second is actin and intermediate filaments, which fill up the cytoplasm .Cytoplasmic actin filaments is otherwise known as the sol-gel zone . Third is the circumferential band of microtubules which encircle the substance of the platelets to form the resting disc like state[32,33].

3.2.8 PLATELET GRANULES AND ORGANELLES

3.2.8 A) PLATELET GRANULES

Any given stimulus need to be amplified or accentuated to get an Adequate platelet functional response. For this, platelets possess certain secretory granule which release stimulatory materials that have been previously sequestered within the resting platelets. Granules are of two types: α granules and dense bodies. They are the main effectors because of their highly reactive and easily available contents [eg:Adenosinediphosphate(ADP) , fibrinogen][34]. The granule secretion initiates with a drastic increase of platelet metabolic activity,

which is started by a wave of calcium release and it is marked by an increased adenosine diphosphate (ADP) synthesis[35,36].

Table : 3

CONTENTS OF THE DIFFERENT GRANULE OF PLATELETS[37]

TYPE OF GRANULE	CONTENTS
Dense granules	**Nucleotides** • Adenine:ATP,ADP • Guanine:GTP,GDP **Amines** • Serotonin • Histamines **Bivalent cations**
Lysosomes	• Glycosidases • Proteases • Cationic proteins

α granules	**<u>Adhesion molecules</u>** • P-selectin(CD62P) • Platelet endothelial cell adhesion molecule- 1 (PECAM-1/CD31). • Glycoprotein IIb/IIIa (GpIIb/IIIa,αIIbβ3 integrin, CD41/61) • Von willebrand factor (vWF) • Thrombospondin-1(TSP-1) • Vitronectin,fibronectin **<u>Mitogenic factors</u>** • Platelet derived growth factor[PDGF] • Vascular endothelial growth factor[VEGF] • Transforming growth factor-β[TGF-β] **<u>coagulation factors</u>** • plasminogen,proteinS,kininogens, fibrinogen. • Factor V,VII,XI,XIII. **<u>Protease inhibitors</u>** • C1 inhibitor • Plasminogen activator inhibitor-1[PAI-1] • Tissue factor pathway inhibitor[TFPI]

3.2.8B) ORGANELLES

Microperoxisomes: rare small (90nm diameter) granules and due to their catalase activity, they can be demonstrated with alkaline diaminobenzidine[38]. It may be involved in synthesis of platelet activating factor. Its final role in the platelet cytoplasm is yet to be found out[39].

Coated vesicles: they are 70 to 90nm in diameter. They are recognized by their electron dense coat. The polyhedral surface coat is formed of clathrin.the coat that is found over the coated pits and vesicles are the same as that on the plasma membrane and SCCS membrane.

Mitochondria: platelet mitochondria are smaller in size but are similar to mitochondria present in other cells. There are about seven mitochondria per platelet. They are the sites for the respiratory chain and the citric acid cycle[41]. Platelets also contain glycogen in small particles or in masses of closely related particles, that play an important role in platelet metabolism[42].

3.2.9 PLATELET FUNCTION

Platelet functions include shape change and spreading, adhesion, aggregation,secretion, procoagulant action, and clot retraction.

Adhesion: following vascular insult, the initial event is platelet adhesion on to the exposed subendothelial matrix. Glycoprotein receptors on platelets ediates this adhesion. This depends upon the rate of shear. Recruitment of circulating platelets onto the thrombus[43]is also due to this adhesion.

Shape change, spreading: activated platelets become spherical.

They extend pseudopodia which helps in attaching to other to other platelets as well as to the blood vessel wall. The transition to a sphere increases its optical density. The termed 'shape -change'is used for this transition. An increase in density may also be due to other causes. So a scanning electron microscopy should support this. Shape change is due to phosphorylation of myosin light chains. An increase in the intracellular calcium ions activate myosin light chain kinase which causes phosphorylation. Inhibition of myosin light chain phosphatase, regulated downstream of Rho kinase[43] also favours phosphorylation.

Aggregation: it is the cross linking of platelets through binding of fibrinogen, or other bivalent or multivalent ligands like vWF to the integrin αIIbβ3 on adjacent cells[43].

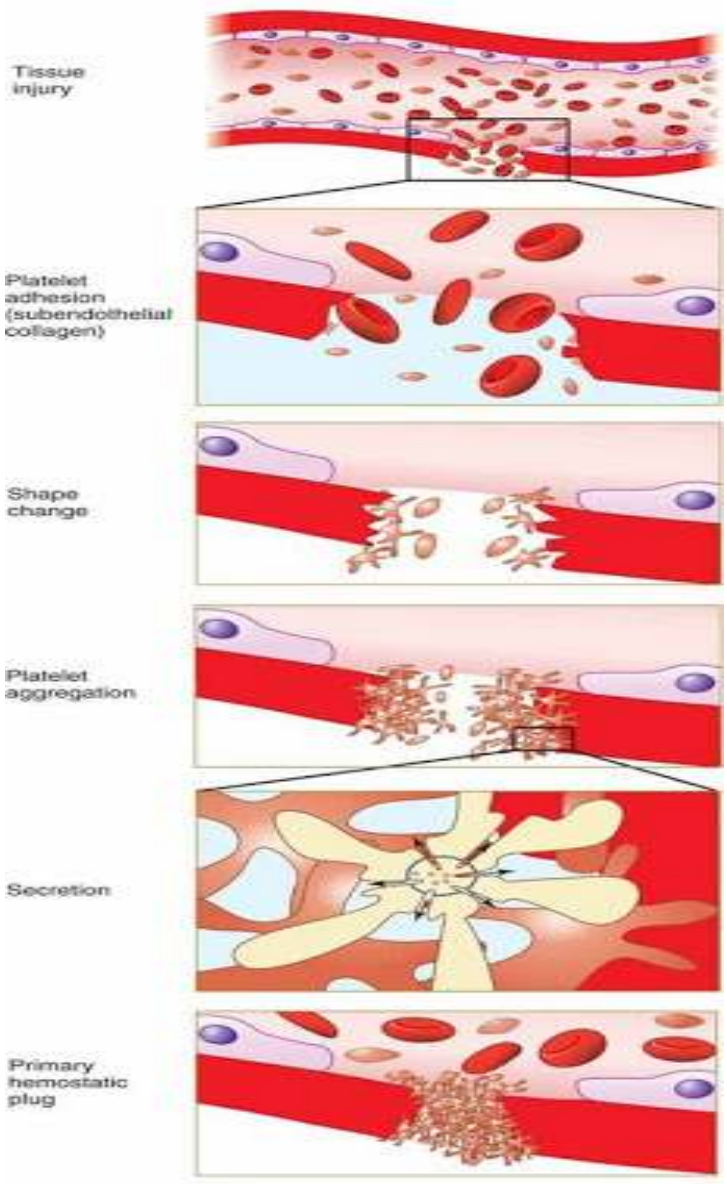


Fig 9:Formation of a Hemostatic Platelet Plug

Secretion: the three forms of granules present in platelets contain differing s contents. These contents play varying roles in haemostasis. A lack of dense or the αgranules forms the basis for heterogeneous group of secretory disorders that are associated with excess bleeding[43].

Procoagulant activity: one of the critical function of platelet activation is to provide a negatively charged phospholipid surface. This negatively charged surface is for the assembly of two multiprotein complexes that are an important part of the coagulation cascade, which include tenase and the prothrombinase complexes. The fraction of the negatively charged surface on the activated platelets is refered to as procoagulant activity or antiphospholipid exposure . It is formed as a result of migration of phosphatidyl serine from the interior to the exterior leaflet of the platelet membrane[43].

Platelet derived microparticles: these are formed during platelet activation. Theyare seen in association with an increase in procoagulant activity. Their formation requires Ca2+ entry.It is seen in response to stimulation by ca2+ ionophore This requires high concentration of agonists and also other favourable

conditions[43] .

clot retraction: blood clots soon after formation retracts over a time period of minutes to hours. The platelet rich thrombi withstands the shear forces in the small arterioles and other blood vessels due to this. Clot retraction can be measured in thrombin- stimulated platelet rich plasma by taking aliquots of the volume of plasma over time after adding thrombin. Thrombin easily generates a clot filling up the aggregometer tube. It gradually reduces to 20% of its initial volume over aperiod of sixty minutes[43].

3.2.10 PLATELET INDICES

Several indices are derived from platelets. The most commonly used are the mean platelet volume (MPV), and the platelet distribution width(PDW). Recent advances have made it possible to measure various platelet parameters like PDW, MPV, PCT, and P-LCR with automated blood cell analysers. These parameters provide important information but are yet to be accepted for routine clinical use[44].

3.3 MEAN PLATELET VOLUME

Measuring the peripheral blood platelet count reveal little about platelet related haemostatic properties unless the count is very low. But, the MPV gives useful clinical as well as patho- physiological information about patients and vascular diseases[8].

3.3.1 PHYSIOLOGY OF PLATELET SIZE

MPV appears to be a marker or determinant of platelet function. In vitro studies have shown that large platelets are more reactive than small platelets. Larger platelets more readily and preferentially aggregate in response to platelet agonists -ADP, collagen, and adrenaline. This produe more prothrombotic and vasoactive substances like arachidonic acid metabolites (eg:thromboxane A2), serotonin, β thromboglobulin and ATP. Larger platelets also have more of dense granules and higher LDH activity[8]. Larger platelets also have a decreased bleeding time which is a measure of invivo haemostatic function[7].

Large platelets also express more of adhesion molecules like P-selectin, GPIIb/IIIa although the surface density remains a constant[8]. MPV correlates with platelet aggregation. This is true with measurements in platelet rich plasma as well as whole blood. The same holds true for population of subjects or in some disease states like diabetes mellitus[8].

3.3.2 THE MEGAKARYOCYTE- PLATELET HAEMOSTASIS - AXIS

Platelets are anucleate cells and have no protein synthetic property. Platelets are heterogeneous with respect to size, density as well as haemostatic capacity. Previously it was thought that platelet size decreases with age. But recent evidence suggest that MPV and other parameters as well as protein content and reactivity are determined mainly at or before thrombopoiesis. MK's are unique mammalian cells in that they are polyploidy, that is they can redouble their chromosomal DNA content without necessarily a subsequent full mitotic

cellular division. This process is called endomitosis. MK's undergo differing numbers of endomitotic cycles producing a population of cells with ploidy ranging from 4N to 128N (2N is the normal diploid state). 16N is the modal ploidy in the majority of mammals studied till date. Each MK synthesises about 1000-2000 platelets, most probably by cytoplasmic fragmentation of MK's in the pulmonary circulation[7].

Measurements of platelet and MK parameters suggest that they can be regarded as a single system: the megakaryocyte- platelet haemostatic axis (MPHA). In normal individuals platelet count is inversely proportional to MPV and

platelet mass, which is a product of MPV and platelet count is a near constant. Also , platelet mass correlates with BT and BT is inversely related to Mk ploidy and size.

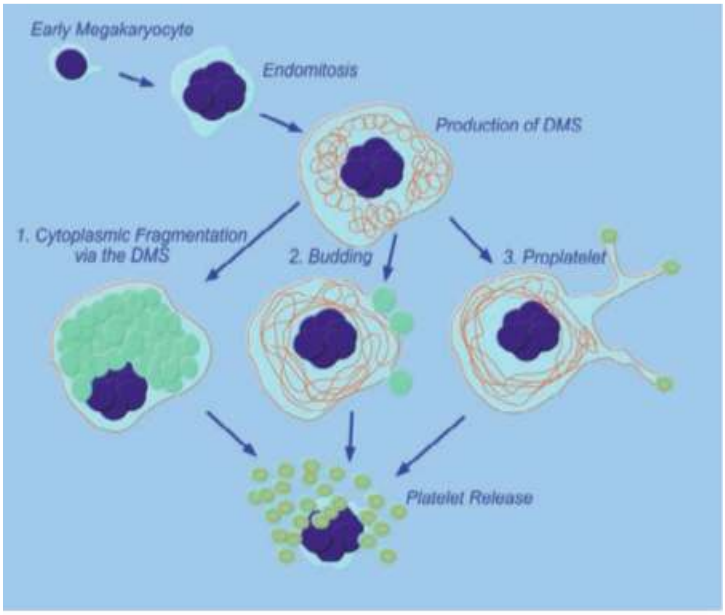


Fig 10: Platelet formation –platelet budding from the megakaryocyte surface, cytoplasmic fragmentation via the demarcation membrane system (DMS), proplatelet formation

When there is an acute platelet destruction without platelet production, MPV increases but the MK ploidy remains the same. When there is only increased platelet production, MK ploidy increases. When both production and destruction coexist, there is an increase in both the MPV as well as the MK ploidy. This signifies that MPV and MK ploidy may change together or independent of each other depending upon the varying haemostatic demands. This has led researchers to think that regulation of MPV and MK ploidy and therefore platelet count are under separate hormonal control. Variations in MPV is due to a change in the rate of platelet destruction but altered MK ploidy and changes in MK size and cytoplasmic volume are due to a change in the rate of platelet synthesis[7].

3.3.3 MEASUREMENT OF PLATELET VOLUME

The best methods for measuring the platelet volume uses changes in the electrical impedance(Coulter haematology analyser) or light diffraction (used by Technicon) ,when a platelet passes through a narrow aperture. Other less satisfactory methods include semiquantitative measurement of diameter on smears or flow cytometry)[8].

In Coulter , cells in fluid suspension are passed through a small opening. A change in voltage proportional to the size of the particle occurs. A raw histogram is then generated and a log-normal curve is fitted to the data. Platelet count is then derived from this MPV is calculated by numerical integration. In sysmex, the cells are hydrodynamically focussed. This is an advantage over coulter. This mechanism ensures that the cells travel along a straight line through the opening. This helps in preventing flow through the edge of the aperture and thereby causing spurious changes in the electrical field. The distribution curve hence obtained is the actual data. It is not a not a fitted curve as in the other. MPV is calculated from the curve using the formula MPV(fL) =pct(%) x1000÷ plt($x10^3/\mu L$).

Laser optic technology is used in Technicon instruments to measure size and granularity of the cells in the suspension. A beam of light is passed through the cells.The amount of forward scatter is proportional to size of the particles .

Side scatter amounts to density or granularity. A histogram is obtained in which MPV is calculated as the mode. Coulter and Technicon results shows 40% difference[1].

Complete blood count specimens are routinely anticoagulated with EDTA which causes platelets to swell on a time dependent basis. Maximam increase in MPV occurs during the first 1.5 hours but it continues over the next 24 hours. EDTA is expected to increase intracellular cyclic AMP and change the plasma membrane permeability[1]. Platelet swelling result in a decreased optical density. So analysers using light diffraction , which measure particle size by assessing optical density, records a reduced MPV value with time. Hence,studies reporting MPV measurements in EDTA sample are of questionable value. This problem can be solved to an extent by measuring MPV at aconsistent time following phlebotomy or after 24 hours when the swelling stops. MPV measured with samples anticoagulated with sodium citrate doesnot change over time[8] and therefore considered gold standard.

3.3.4 NORMAL MPV VALUES

The normal range is yet to be correctly established. Studies measuring MPV in samples anticoagulated with sodium citrate suggest a normal range of 4.5-8.5 fL with a mean of 6.5fL[8]. the day to day variation in MPV is small (CV=2.1%) when compare with platelet count (CV=6.1%)[8]

3.3.5 MPV AND STROKE

In some pathological conditions, the MPHA is acutely or chronically perturbed leading to the formation of hyperfunctional platelets, resulting in vascular disease or thrombotic events like stroke. There is evidence supporting accentuated platelet function in acute ischemic stroke[7].

The basic issue to be addressed is whether the increased platelet function precedes the onset of stroke thereby playing a causative role or whether it is a reactive change . Information on this is gathered by studying MK's and platelets in the acute stage (within 36 hours of onset). MPV measured at this stage may well reflect the potential reactivity of platelets prior to the occurrence of the stroke. Since the dynamics of platelet consumption and production in the acute phase of ischemic stroke are still under study, it is impossible to fully rule out the fact that MPV is modified by the acute destruction of platelets and subsequent changes in the fragmentation of MK cytoplasm. If MK parameters can be shown to be abnormal immediately following the occurrence of stroke,

it would be strongly suggestive of a chronic perturbation of MPHA before the occurrence of stroke[7].

Stroke risk factors like diabetes mellitus, hypertension, smoking and hypercholesterolemia, and in certain vascular conditions associated with stroke , such as atherosclerosis and myocardial infarction have shown an icreased platelet function leading to a shift in the MK indices in a prothrombotic irection . So it seems possible that in patients with certain risk factors , systemic platelet activation precedes stroke[7].

There have been many studies correlating MPV and ischaemic stroke. O'malley et al studied 58 patients. Platelet variables were assayed in the acute (<48 hours of stroke) and chronic(>6 months) phases of ischaemia and compared it to that of age and sex matched controls. MPV was found to be higher in cases than in the controls. He also showed that MPV showed no significant change from the acute phase in those who survived. The study thus concluded that there is an increase in MPV and reduced platelet count in acute ischemic stroke and that it persist long after acute event. These observations are suggestive of a role of larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis[1].

A substudy of The Perindopril Protection Against Recurrent Stroke Study [PROGRESS] was done by Philip Bath et al[4] . 3134 cases of this study were followed up for an average time period of 3.9 years to assess the correlation

between MPV and ischaemic stroke. The study population had a mean age of 65 years and 71% were males. The average MPV was found to be 10.0 fL. The study concluded a positive orrelation between MPV and risk of stroke. There was a 11% increased relative risk of stroke per femtoliter increase in MPV. Perindopril donot alter MPV. The study concluded MPV as an independent predictor of risk of stroke amongst individuals with a prvious history of stroke . Therefore measuring MPV may be useful prognostically in patients with a previous history of cerebrovascular disease[4]. There are few similar studies supporting and refuting the association between MPV and ischaemic stroke.

3.3.6 MPV AND ANTIPLATELET DRUGS

Platelet aggregation is an important step in hemostasis and is involved in vascular events like atherosclerosis, arterial thromboembolism, unstable angina, myocardial infarction, transient ischemic attacks and stroke[48]. Inhibition of platelet aggregation by antiplatelet drugs like aspirin has become important in the treatment of above conditions. Aspirin irreversibly inhibits cyclooxygenase and inhibits platelet aggregation. It is still not clear whether this impairment of function due to aspirin influences the feedback control of platelet production and therefore the platelet count and platelet volume. Studies have shown that aspirin may affect the circulatory platelet mass under certain conditions[48].

3.3.7 MPV AND AGE

Though the previous thinking was that platelet size decreases with age,recent research contradicts this. Recent data is in favour of the fact that MPV and other related platelet parameters and therefore the platelet protein content as well as reactivity are determined mainly during or before thrombopoiesis by MK[9].

3.3.8 MPV AND GENDER

Few studies have shown gender dependent variations in platelet count with women having higher counts than men. This might reflect the different hormonal profiles or the compensatory effect associated with menstrual blood loss. Studies have shown no statistically significant differences in MPV in males and females[49]

3.3.9 MPV AND HYPERTENSION

MPV is shown to be significantly higher in hypertensives than in normotensives in some studies, but no such differences were seen for platelet counts[50.]

3.3.10 MPV AND DIABETES MELLITUS

MPV is found to be significantly higher in patients with diabetes mellitus and those with impaired fasting glucose than normal individuals [51].

3.3.11 MPV AND METABOLIC SYNDROME

The mean MPV of subjects with biochemical markers suggestive of the metabolic syndrome, according to the Adult Treatment Panel(ATP) III criteria, is slightly higher but not significant[52].

3.3.12 MPV AND SMOKING

Tobacco smoking is known to accelerate atherosclerosis. Smoking generates free radicals which breakdown NO, which on one hand increases thromboxane production (prothrombotic action), but on the other hand decreases prostacyclin synthesis (antithrombotic action). This leads to clotting disorder. Smoking does not have an effect on MPV or platelet count[53].

3.3.13 MPV AND ISCHAEMIC HEART DISEASE

Larger platelets, being haemostatically more active, are a risk factor for coronary thrombosis[54]

Materials and methods

4.MATERIALS AND METHODS

4.1 SETTING OF THE STUDY

The study was a prospective study conducted at Coimbatore Medical College, a tertiary care centre and data was collected over a period of six months from December 2013 to may 2014. The study was conducted amongst 100 patients diagnosed with acute ischemic stroke and who presented to the hospital within 48 hours of onset of symptoms. Hundred controls were also selected. Controls were matched for age, sex,known risk factors including hypertension, diabetes, dyslipidemia, smoking,and alcoholism. The study was approved by the institutional ethics committee.

4.2 STUDY DESIGN

The study conducted was a case control study.

Cases definition: rapidly developing clinical symptoms or signs of focal or global loss of cerebral function with symptoms lasting for more than 24 hours or leading to death with no apparent cause other than that of vascular origin (WHO definition).

Cases included in the study were patients admitted in the medical wards who were diagnosed to have stroke based on the above definition and who met the inclusion criteria.

Inclusion criteria:

1)Gender: male/ female

2) Age range: >20 years

3) Socioeconomic status: all socioeconomic groups were included.

Exclusion criteria:

1) Thrombocytopenia
2) Known cases of hereditary disorders of large platelets
3) Haemorrhagic stroke
4) Medications reducing platelet count like hydroxyurea, antineoplastic agents.
5) Patients on antiplatelet medication like aspirin, clpidogrel.
6) Patients presenting to the institution 48 hours after the onset of the Symptoms.
7) Peripheral smear showing platelet aggregates.
8) Patients unable to communicate as a result of severe stroke or aphasia without a valid surrogate respondent (valid surrogate respondent is a spouse or first degree relative living in the same home or is self identified as aware of patient's previous medical history and current treatment)

Controls:

Controls were selected from amongst those patients admitted in the

medical wards for other diseases. Each control was matched for age(+/-5), sex, risk factors for stroke like diabetes mellitus, hypertension, smoking, alcoholism, and dyslipidemia. There was one control for each case recruited.

Inclusion criteria:

1) Patients admitted to the medical wards for other diseases
2) Patients attending the outpatient clinic

Exclusion criteria:

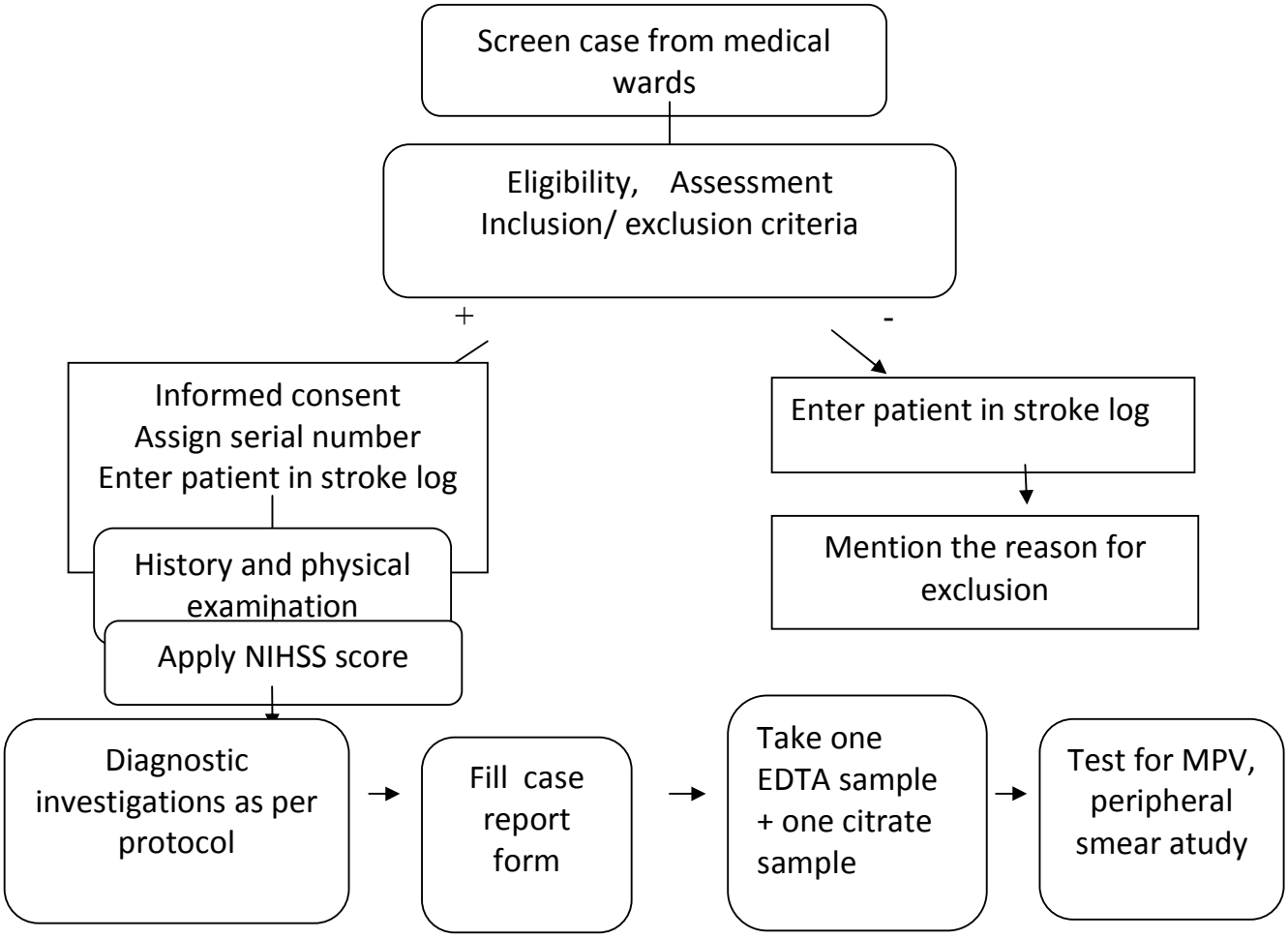
1) Thrombocytopenia
2) Peripheral smear showing platelet aggregates
3) Known cases of hereditary disorders with large platelets
4) Individuals on antiplatelet drugs
5) Individuals on drugs like hydroxyurea, antineoplastic agents, that reduce platelet counts

4.3) Method of data collection

All stroke patients admitted to Coimbatore Medical College during the time period described above were assessed. Each of them were entered into a stroke log. Patients fulfilling the inclusion criteria were enrolled into the study, after obtaining an informed consent. Data was collected and recorded as per the proforma. Each patient was allotted a serial number and included into the study

as a case. Each case was assessed and severity of stroke assessed using the NIHSS. Blood sample was collected from the antecubital vein using a 5cc syringe. Sample was then transferred to both EDTA and citrate vacutainers. The samples were taken to the institutional laboratory between 2 hours and 4 hours of collection. Samples were analysed using Sysmex automated analyser which uses the technology based on electrical impedance to measure the MPV. Peripheral smear study was also done for each sample taken to rule out the presence of platelet aggregates. Patients with samples showing platelet aggregates were excluded from the study. The same procedures were carried out for obtaining samples from controls and were transferred to EDTA and citrate vacutainers. The samples were analysed using the same autoanalyser. Peripheral smear study was also carried out for each sample collected to look for the presence of platelet aggregates and if present were excluded.

4.4 SOP for cases



4.5)PRINCIPLE BEHIND ESTIMATION OF MPV WITH SYSMEX AUTOMATED HEMATOLOGY ANALYSER

RBC/ PLATELET DETECTION PRINCIPLE

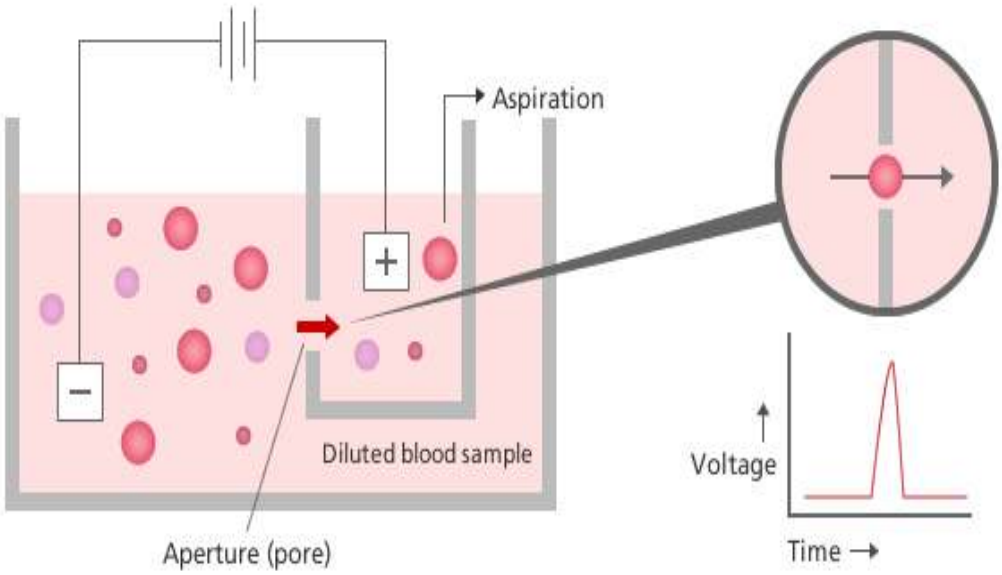


Fig:10 principle behind automated hematology analyser

The principle used is cell counting by electric impedance method. Impedance variation generated as a result of movement of cells through a caliberated micro aperture is measured. The specimen is diluted in an electrolytic diluent (current conductor) and pulled through the calibrated microaperture. Two electrodes are placed on either side of the aperture. Electric current passes through the electrodes continuously. When the cell passes through the aperture, electric resistance between the two electrodes increases proportionately with the cell volume. The generated impulses have a very low voltage, which the amplification circuit increases, so that the electronic system can analyze them.

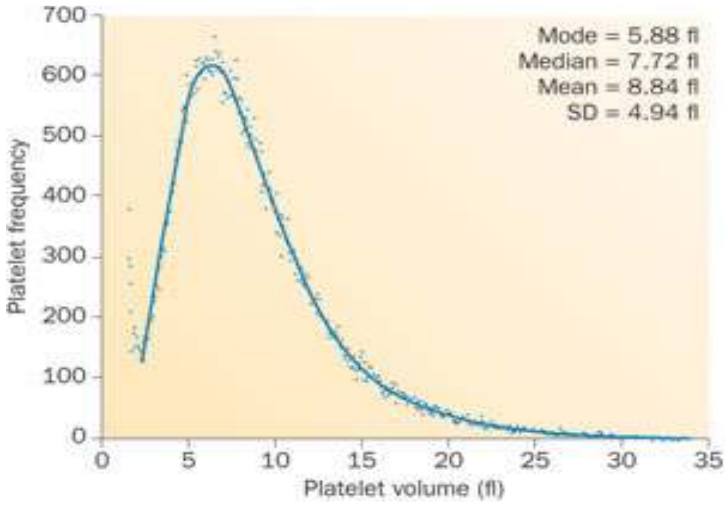


Fig 11: Log Gaussian platelet volume distribution curve

The MPV is directly derived from the analysis of the platelet distribution curve. The volume of each platelet is plotted on a histogram and the mean of it is taken.

4.6 THE NATIONAL INSTITUTES OF HEALTH STROKE SCALE USED TO ASSESS THE CLINICAL SEVERITY OF STROKE[55,56]

4.6 THE NATIONAL INSTITUTES OF HEALTH STROKE SCALE USED TO ASSESS THE CLINICAL SEVERITY OF STROKE[55,56]

SCORE	SEVERITY OF STROKE
0	No stroke symptoms
1-4	Minor
5-15	Moderate
16-20	Moderate to severe
21-42	Severe

Performing the scale

1. Level of Consciousness

    1 (A) level of consciousness - Responsiveness

    1(B) level of consciousness -Questions

    1(C) level of consciousness -Commands

2. Horizontal Eye Movement

3. visual

4. Facial Palsy

5. Motor Arm

6. Motor Leg

7.Limb Ataxia

8.Sensory

9.Best Language

10.Speech

11.Extinction and Inattention

1.LEVEL OF CONSCIOUSNESS

A.RESPONSIVENESS

The investigator must choose a response if a full evaluation is prevented by obstacles like endotracheal tube, orotracheal trauma/bandages,and language barrier. A score of 3 is made only if the patient makes no movement (apart from reflexive posturing) in response to noxious stimulation.

score	Test results
0	Alert; keenly Responsive
1	Not alert; but verbally arousable or aroused by minor stimulation to obey, answer, or respond.
2	Not alert; Only responsive to repeated or strong and painful stimuli
3	Totally unresponsive, flaccid, and areflexic; or Responds only with reflex motor or autonomic effects

B.QUESTIONS

The patient is asked the month and the patient's own age. The answer must be correct. There is no credit at all for being close to the right answer. Aphasic and stuporous patients who do not comprehend the questions should be assigned a score 2. A score of 1is given if the patient is not able to speak due to causes such as endotracheal intubation, orotracheal trauma, severe dysarthria from any cause, language barrier, or any other problem not secondary to aphasia . Only the initial answer be graded and the examiner should not "help" the patient with verbal or non-verbal cues.

SCORE	TEST RESULTS
0	answers both questions accurately
1	answers onlyone question correctly
2	Does not correctly answer either question

C.COMMANDS

The patient is asked to first open and close the eyes and then to grip and release the non-paretic hand. Substitute this with another one step command if the patient is unable to use both hands . Credit is given if an unequivocal attempt is made but could not complete due to weakness. If the patient does not respond to the command, the task should be demonstrated (pantomime), and the result scored (i.e., follows none, one or two commands). Patients with trauma, amputation, or other physical impairments should be given suitable one-step commands. The first attempt alone is scored .

SCORE	TEST RESULTS
0	performs both tasks accurately.
1	Correctly performs 1 task.
2	Performs neither task correctly.

Only horizontal eye movements are tested. Voluntary or reflexive (oculocephalic) eye movements are scored, but caloric testing is not done. If the patient has a conjugate deviation of the eyes which is overcome by voluntary or reflexive activity, the score is 1. Patient with an isolated peripheral nerve paresis (cranial nerves III, IV or VI) scores 1. Patients with ocular trauma, bandages, pre-existing blindness, or other disorder of visual acuity or visual fields are to be tested with reflexive movements, and a choice is to be then made by the investigator. Gaze is testable in all aphasic patients. . Establishing eye contact and then moving about the patient from side to side may sometimes clarify the presence of a partial gaze palsy

2.HORIZONTAL EYE MOVEMENT/BEST GAZE

SCORE	TEST RESULTS
0	Normal
1	Partial gaze palsy; gaze is abnormal in one or both eyes, but gaze is not totally paralyzed. Patient can gaze towards hemisphere of infarct,but can go past midline
2	Forced deviation -gaze is fixed to one side, or total gaze paresis not overcome by the oculocephalic maneuver

3.VISUAL FIELD TEST

Visual fields (both upper and lower quadrants) are tested by confrontation, finger counting or visual threat,whichever is appropriate. Patients may be encouraged, but if they look towards the side of the moving fingers appropriately, it can be scored as normal. If there is unilateral blindness or enucleation, visual field in the remaining eye is scored. Score 1 only if there is a clear-cut asymmetry, including quadrantanopia. Patient blind from any cause is assigned a score 3.

SCORE	TEST RESULTS
0	No loss
1	Partial hemianopia or complete quadrantanopia
2	Complete hemianopia
3	Bilateral Blindness, includes blindness from any cause

4. FACIAL PALSY

Ask (use pantomime if required to encourage) the patient to show teeth or raise eyebrows and close eyes. symmetry of grimace in response to noxious stimuli is scored in the poorly responsive or non-comprehending patient.Physical barriers that obscure the face like facial bandages, orotracheal tube, tape etc should be removed to the possible extent.

SCORE	TEST RESULTS
0	Normal , symmetrical movements
1	Minor paralysis such as flattened nasolabial fold or minor asymmetry on smiling
2	Partial paralysis; particularly paralysis in lower face - total or near-total paralysis of lower face
3	Comple paralysis, absent movements in upper and lower face

5.MOTOR ARM

The limb is held in the correct position: extend the arms (palms down) to 90 degrees (sitting) or 45 degrees (supine). Drift is scored if the arm falls before 10 seconds. The aphasic patient is encouraged as required using urgency in the voice as well as pantomime, but noxious stimulation is not used. Each limb is tested , beginning with the non-paretic arm. In the case of amputation or if there is joint fusion at the shoulder, the examiner records the score as untestable (UN) and records explanation for the same.

SCORE	TEST RESULTS
0	No drift; the arm remains in the initial position for the full 10 seconds
1	Drift; the arm drifts to an intermediate position prior to the end of the full 10 seconds but does not hit the bed or other support .
2	Little effort against gravity; drifts down to a physical support prior to the end of the 10 seconds
3	No effort against gravity; the arm falls immediately to the initial position, but there is some movement of the arm (e.g. shoulder shrug)
4	No movement/ no ability to enact voluntary movement UN- amputation or joint fusion—explanation 5a left arm , 5b- right arm

6.MOTOR LEG

The limb is positioned at 30 degrees (always tested supine). Drift is scored if the leg falls before 5 seconds. The aphasic patient is encouraged as required using urgency in the voice or pantomime, but noxious stimulus is not used. Each

limb is tested , beginning with the non-paretic leg. In the case of amputation or joint fusion at the hip, the examiner record the score as untestable (UN)and write the explanation for the same.

SCORE	TEST RESULTS
0	No drift; the leg maintains the initial position for the full 5 seconds
1	Drift; the leg drifts prior to the end of the full 5 seconds, but does not at any point touches the bed for support.
2	some effort against gravity is present; leg drifts down from the initial position to a physical support prior to the end of 5 seconds
3	No effort against gravity/ the leg falls immediately after being positioned to the testing posture.
4	No movement UN-amputation/ joint fusion,--explanation 6a-left limb, 6b- right limb

7. LIMB ATAXIA

It is aimed at detecting unilateral cerebellar lesion. It is tested with eyes open. If visual defect is present, ensure that testing is done in the intact visual field. The finger-nose-finger and the heel-shin tests are performed on both sides,

and ataxia is scored only if it is out of proportion to the weakness. Ataxia is absent in the patient who cannot understand or is paralyzed. In case of amputation or joint fusion, the examiner records the score as untestable (UN), and write the explanation for this. In case of blindness, test by making the patient touch his nose from extended arm position.

SCORE	TEST RESULTS
0	Absent ,Normal coordination
1	Ataxia present in one limb
2	Ataxia present in 2 limbs: rigid and inaccurate movement in both limbs on one side

8.SENSORY

Sensation or grimace to pinprick or withdrawal from noxious stimulus in the obtunded or aphasic patient is tested. Only the sensory loss attributed to stroke is scored as abnormal . As many body areas (arms [not hands], legs, trunk, face) as needed to accurately check for hemisensory loss should be tested. Patients with brainstem stroke who has bilateral loss of sensation is scored 2. If the patient does not respond and is quadriplegic, score 2 is given. Patients in coma (item 1a=3) are given a score of 2.

SCORE	TEST RESULT
0	Normal,no evidence of sensory loss
1	Mild-to-Moderate sensory loss present; patient feels the pinprick but it is dull on the affected side.
2	Severe to total sensory loss present; patient is not aware of being touched over face, upper and lower limbs on the affected side.

9. BEST LANGUAGE

The patient is asked to describe the attached picture, to name the items on the attached naming sheet and also to read from the attached list of sentences. Comprehension is judged not only from responses here but also from the preceding neurological examination. If visual problems interfere with the tests, ask the patient to identify objects placed in hand, repeat, and produce speech. The intubated patient should be asked to write. The patient in coma will score 3 on this item. The examiner must choose a score for the patient with stupor or limited

cooperation, but a score of 3 should be used only if the patient is mute and follows no one-step commands.

SCORE	TEST RESULT
0	Normal; no obvious speech deficit
1	Mild-to-moderate aphasia - detectable loss in fluency, but information can be extracted from the patient's speech
2	Severe aphasia- all speech is fragmented, examiner is unable to extract the figure's content from the patients speech.
3	Unable to speak or understand speech, mute,global aphasia

10. SPEECH

If the patient is thought to be normal, an adequate speech must be obtained by asking the patient to read or repeat words from the attached list. If the patient has severe aphasia, the clarity of articulation of spontaneous speech can be rated. If the patient is intubated or has other physical barriers to producing speech, the examiner records the score as untestable (UN), and clearly records an explanation for this .

SCORE	TEST RESULTS
0	Normal; clear and smooth speech
1	Mild-to-moderate dysarthria present; some slurring of speech is present,however the patient can be understood
2	Severe dysarthria present; speech is so slurred that he or she cannot be understood, or unable toproduce any speech UN= intubated/ other physical barrier---explanation

11. EXTINCTION AND INATTENTION(FORMERLY NEGLECT):

Sufficient information to identify neglect would have been obtained from prior testing. If the patient has a severe visual loss preventing visual double simultaneous stimulation, and the cutaneous stimuli are normal, the score is normal. If the patient has aphasia but does appear to attend to both sides, the score is normal. The presence of visual spatial neglect or anosagnosia may be taken as an

evidence of abnormality. Since the abnormality is scored only if present, the item is never untestable.

SCORE	TEST RESULTS
0	Normal
1	Inattention in one of the sensory modality-- visual, tactile, auditory, or Spatial
2	Profound hemi-inattention or extinction to more than one modality - does not recognize own hand or orients to only one side of space

4.7 INVESTIGATIONS USED FOR CASES AND CONTROLS

INVESTIGATIONS	CASES	CONTROLS
PLATELET COUNT	YES	YES
MPV	YES	YES
PERIPHERAL SMEAR	YES	YES
RANDOM BLOOD SUGAR	YES	YES
LIPID PROFILE	YES	YES
CT/MRI BRAIN	YES	NO

4.8 STATISTICAL METHODS

Sample size: 100 cases admitted in the medical wards of Coimbatore Medical College, who gave consent and who met the inclusion criteria were included. 100 controls were also selected.

Data analysis: The statistical software SPSS (version18) was used for data analysis. Microsoft word and excel have been used to generate graphs and tables.

Statistical methods:

Descriptive statistical analysis has been carried out in this study. Results on continuous measurements are expressed as Mean±SD (min-max). Results on categorical measurements are expressed as number(%). Significance is assessed at 5% level of significance. Analysis of variance (ANOVA) has been used to find the significance of study parameters between three or more groups of patients, Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups. A multivariate logistic regression analysis has been used to find out the risk factors associated with stroke[60,61,62and63.]

1) Analysis of variance - ANOVA
2) Student T test(two tailed, independent)[63]
3)Significant figures

+ suggestive of significance (p value: $0.05 < p < 0.10$)

*moderately significant (p value: $0.01 < p \leq 0.05$)

**Strongly significant (P value : $p \leq 0.01$)

DEMOGRAPHIC DATA

472 Stroke patients admitted to the medical wards were screened to get 100 cases.

TABLE 4: STROKE LOG AND REASONS FOR EXCLUSION

NO OF CASES SCREENED	472
NO OF CASES INCLUDED	100
NO OF CASES EXCLUDED	372

REASONS FOR EXCLUSION

Reason for exclusion	**number**	**Percentage(%)**
Late presentation to hospital (>48hrs)	172	46.2
Hemorrhagic stroke	60	16.1
Delay in recruiting	62	16.7
Platelet aggregates on peripheral smear	22	5.9
No informed consent	56	15.1

CHART 1: STROKE LOG AND REASONS FOR EXCLUSION

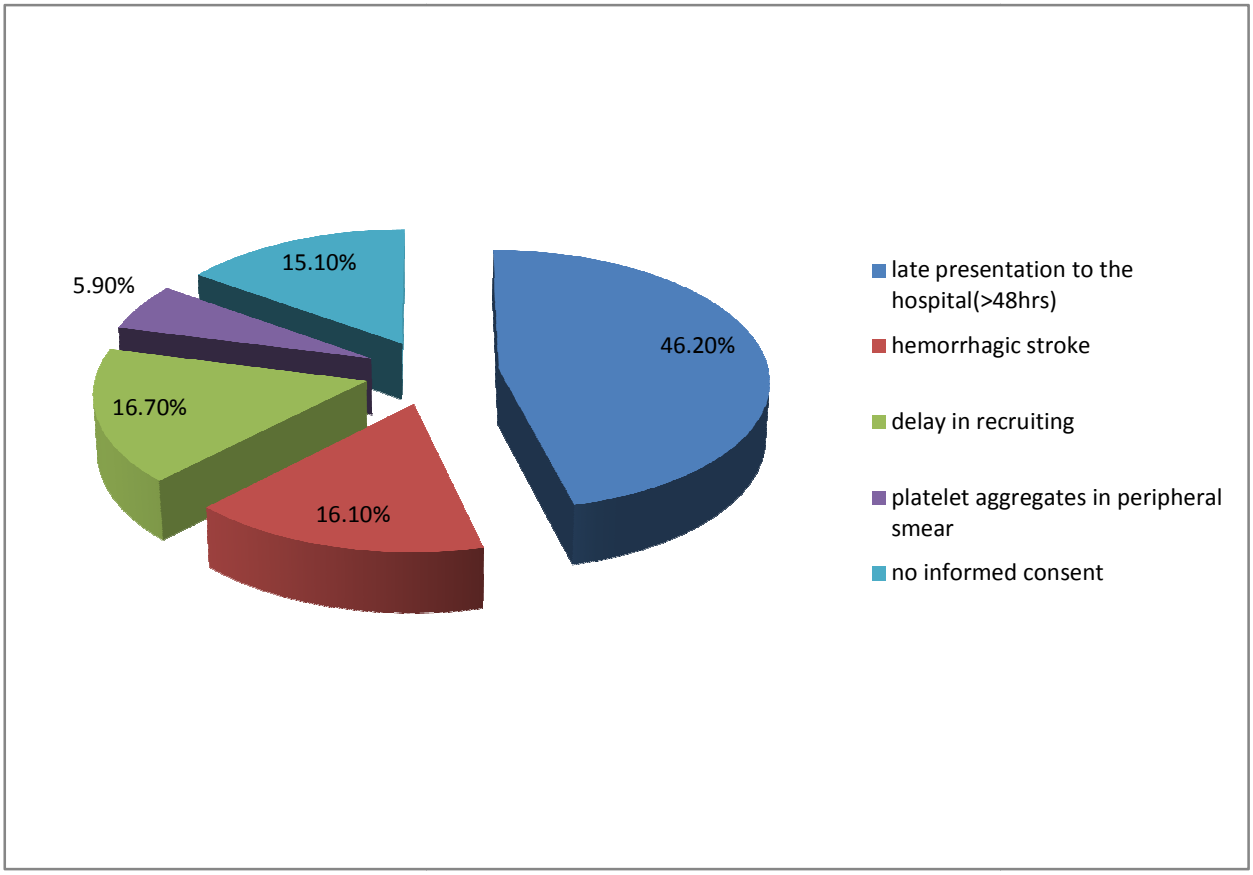


TABLE 5: AGE DISTRIBUTION

AGE IN YEARS	CASES		CONTROLS	
	NO	%	NO	%
21-30	4	4	4	4
31-40	8	8	8	8
41-50	12	12	12	12
51-60	36	36	36	36
61-70	26	26	26	26
71-80	12	12	12	12
>80	2	2	2	2
TOTAL	100	100	100	100
MEAN±SD	57.08±13.31		57.21±13.23	
MALE	55.62±12.74		55.85±12.60	
FEMALE	61.23±14.25		61.08±14.45	
P value	0.064		0.083	

The samples are age matched with p=0.944

The mean age for cases was 57.08±13.31, whereas for controls it was 57.21±13.23. the maximum number of cases in this study were in the age group

between 51 & 60, followed by 61 -70. The youngest age was 24 for cases and 23 for controls. The oldest age was 83 for cases and 84 for controls.

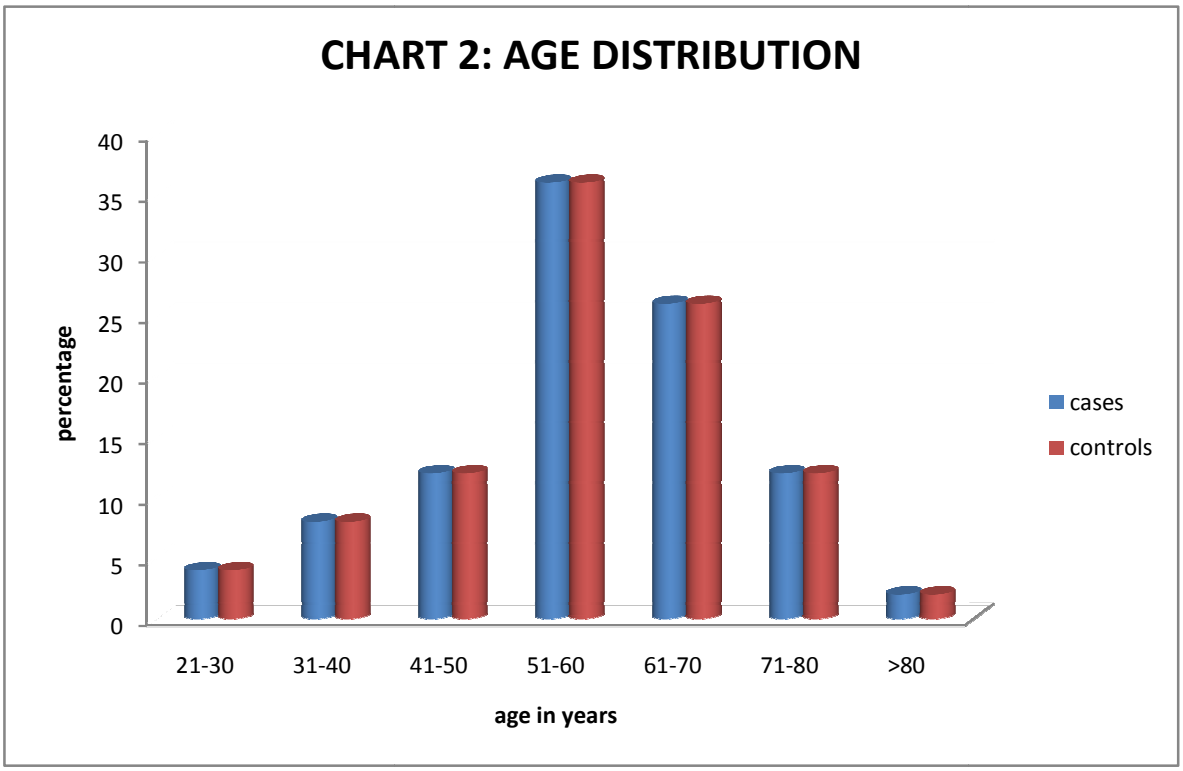


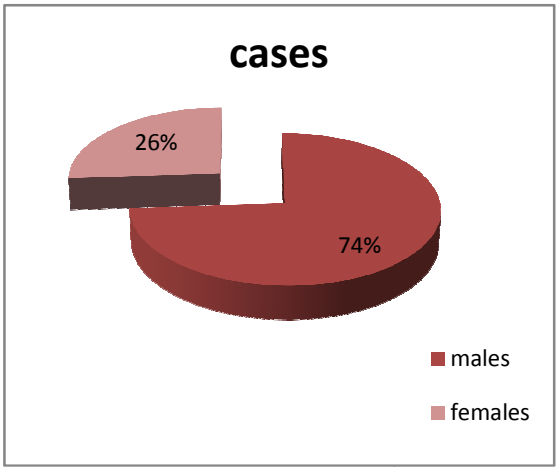
TABLE 6: GENDER DISTRIBUTION

74% of cases and controls were males and 26% were females. Females (61.23±14.25) with stroke were older than males (55.62±12.74) , but this was not found to be statistically significant

GENDER	CASES		CONTROLS	
	NO	%	NO	%
MALE	74	74	74	74
FEMALE	26	26	26	26
TOTAL	100	100	100	100

Samples are gender matched with p=1.000

CHART 3: GENDER DISTRIBUTION



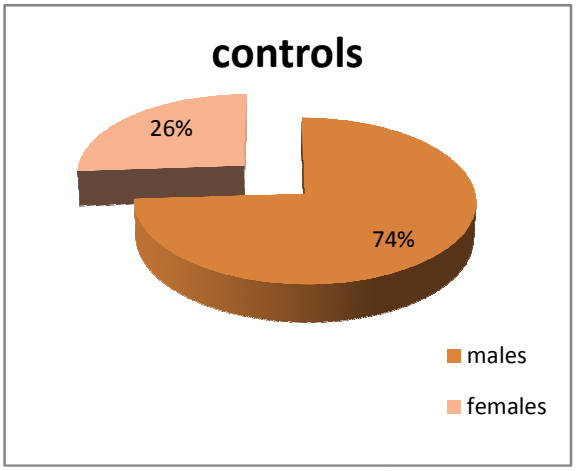


TABLE 7:RISK FACTOR PROFILE

Out of the many risk factors for stroke, hypertension was the most prevalent in this study group with a percentage of 53. Dyslipidemia came second with a percentage of 33%. Diabetes came third.

RISK FACTORS	CASES		CONTROLS		P value
	NO	%	NO	%	
DIABETES MELLITUS	29	29	29	29	1.000
HYPERTENSION	53	53	53	53	1.000
DYSLIPIDEMIA	33	33	33	33	1.000
SMOKING	25	25	23	23	0.741
ALCOHOLISM	28	28	28	28	1.000
CORONARY ARTERY DISEASE	9	9	7	7	0.019
PREVIOUS STROKE	4	4	3	3	0.121

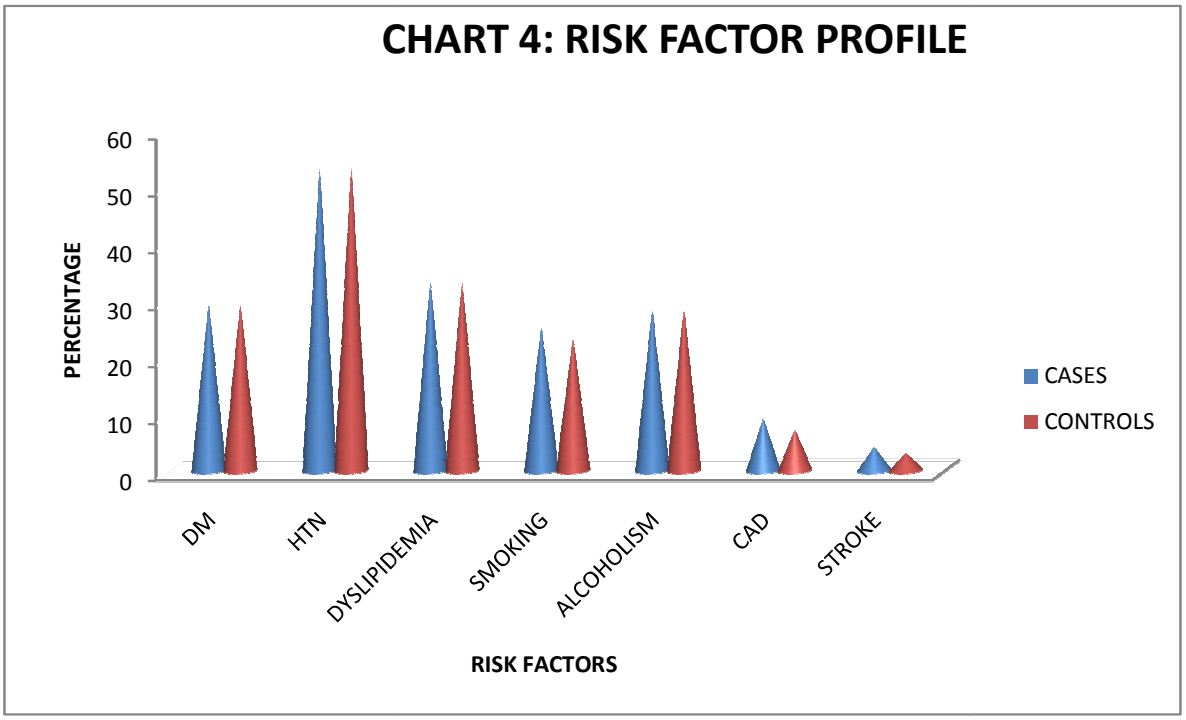


TABLE 8: CLINICAL PROFILE

CLINICAL MANIFESTATIONS	NO	%
Hemiplegia (motor), facial palsy	53	53
Hemiplegia (motor+ sensory)	21	21
Hemiplegia, facial palsy, homonymous hemianopia, aphasia	6	6
Monoplegia	8	8
Cerebellar signs	12	12

CHART 5 CLINICAL PROFILE

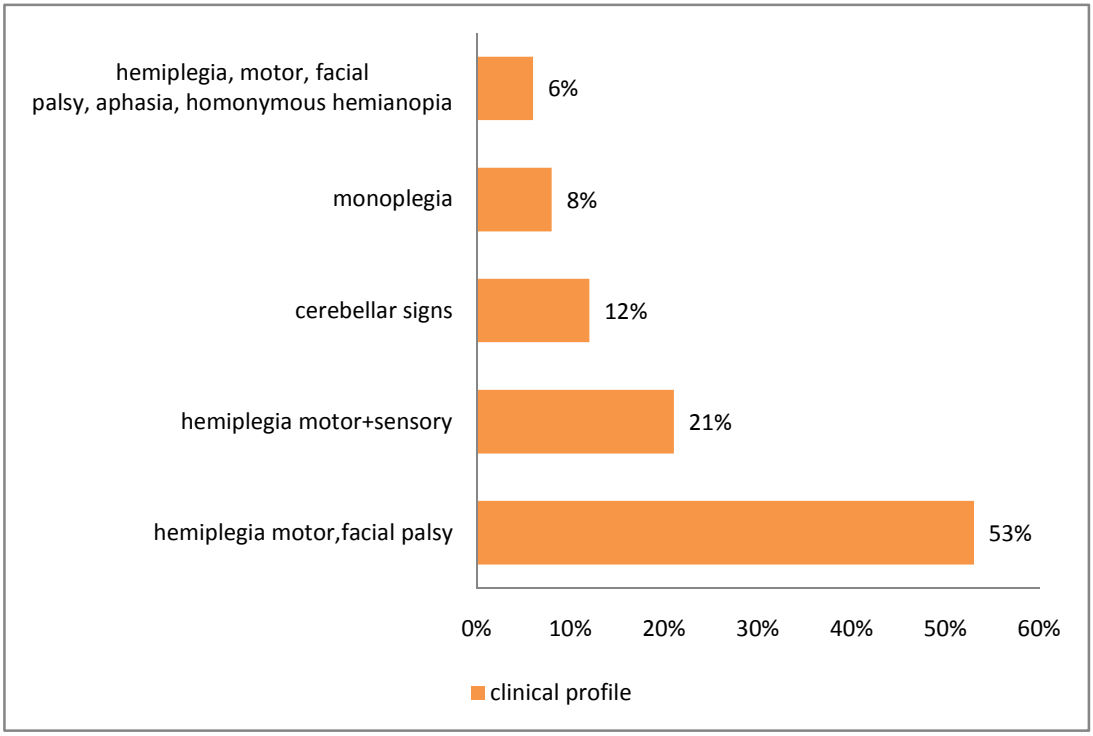


TABLE 9

THE OXFORDSHIRE COMMUNITY STROKE PROJECT CLASSIFICATION OF STROKE SYNDROMES

The classification subtyped strokes on the basis of clinical criteria. Predominant subtype was lacunar syndromes which accounted for 66% of total cases, followed by POCS and PACS with 24 % and 8% each.

STROKE SUBTYPE	**NO**	**%**
LACS (LACUNAR SYNDROME)	66	66
POCS (POSTERIOR CIRCULATION SYNDROME)	24	24
PACS (PARTIAL ANTERIOR CIRCULATION SYNDROME)	8	8
TACS (TOTAL ANTERIOR CIRCULATION SYNDROME)	2	2

CHART 6 STROKE SUBTYPES

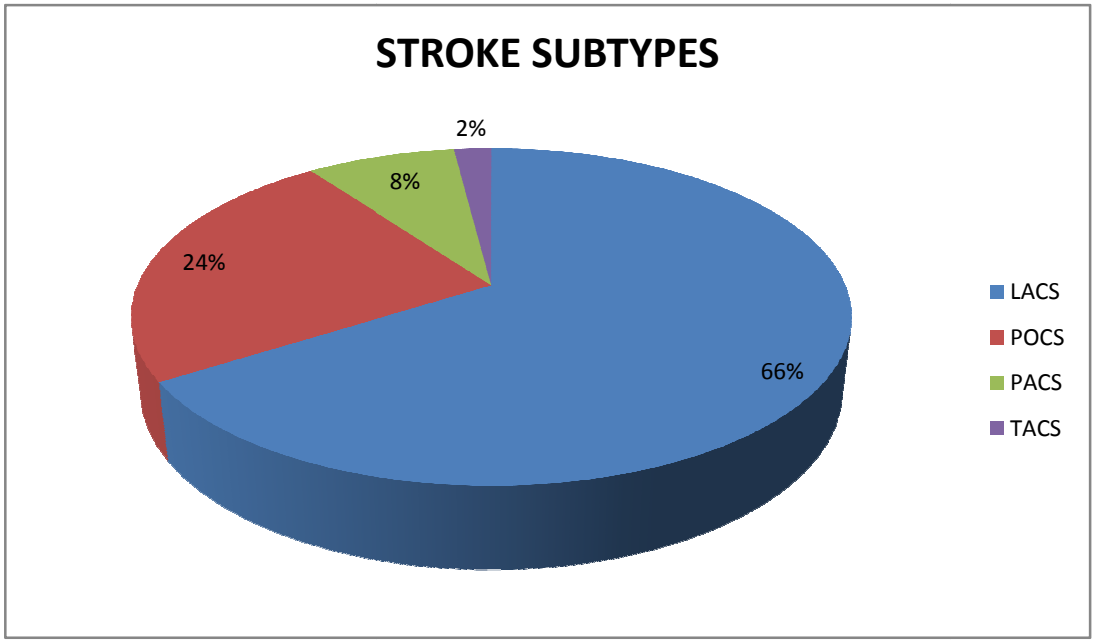


TABLE 10 : STROKE CLINICAL SEVERITY SCORE

NIHSS	NO	%
MINOR (1-4)	3	3
MODERATE (5-15)	29	29
MODERATE- SEVERE (16-20)	21	21
SEVERE (21-42)	47	47

CHART 7 STROKE SEVERITY

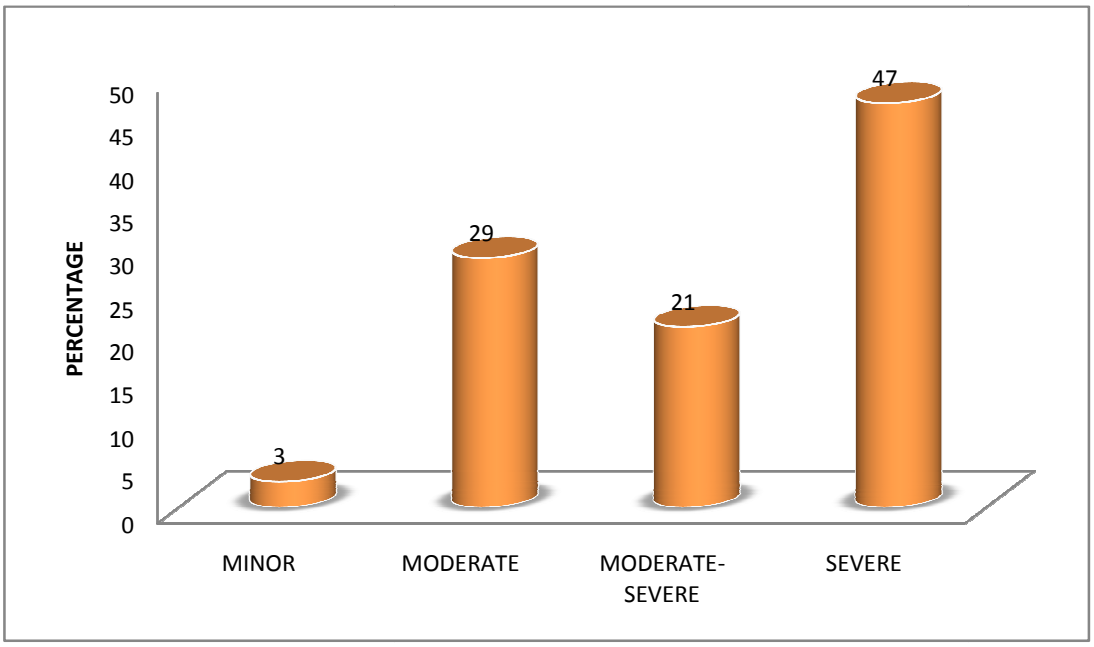


TABLE 11 :COMPARISON OF PLATELET COUNTS IN CASES AND CONTROLS

There was a trend for lower platelet count in cases, but this was not statistically significant (p= 0.178). platelet count in cases averaged 275040±123609 and that in controls averaged 298670± 123666.

PARAMETER	CASES	CONTROLS	SIGNIFICANCE
PLATELET COUNT	275040±123609 (1,00,000-5,44,000)	298670±123666 (1,00,000-5,18,000)	t=-1.351 P= 0.178

Results are expressed as MEAN± SD (min-max)

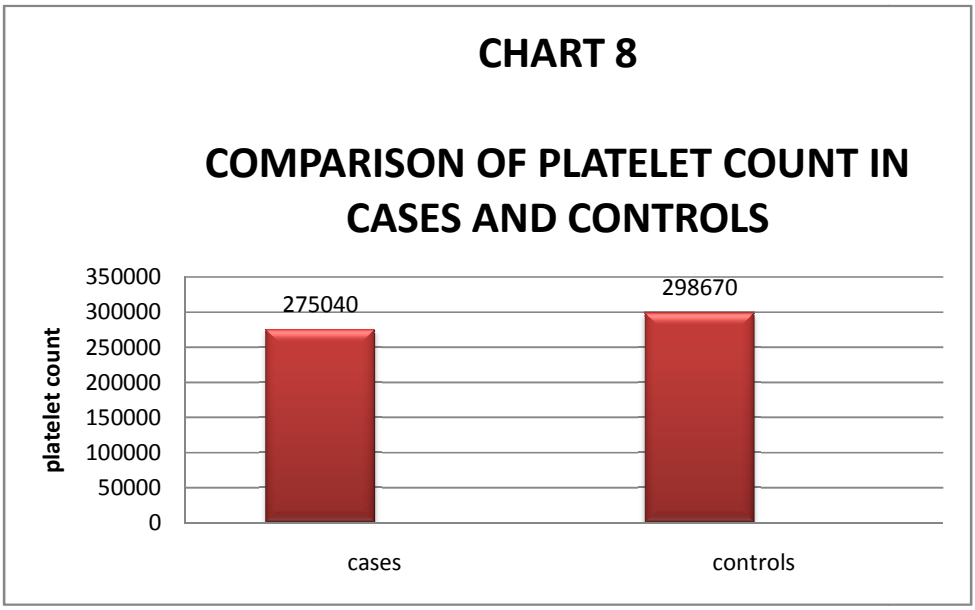


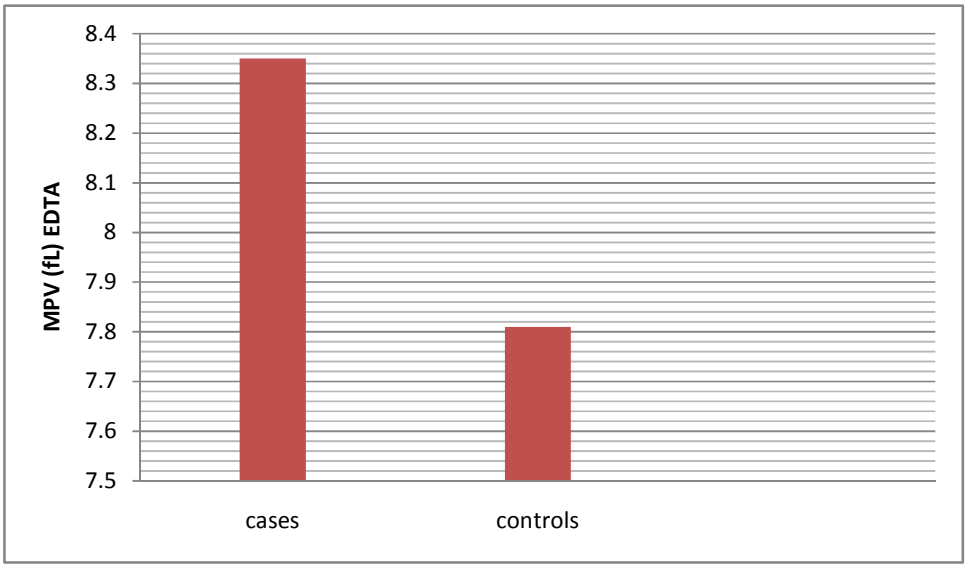
TABLE 12: COMPARISON OF MPV IN CASES AND CONTROLS

MPV(fL)	CASES	CONTROLS	SIGNIFICANCE
EDTA	8.35±0.98 (6.4-10)	7.81±0.79 (5.9-9)	t=4.283 p= < 0.001**
CITRATE	7.93±0.99 (6.1-9.6)	7.30±0.74 (5.8-8.9)	t=5.048 P=<0.001**

Results are expressed as MEAN ±SD (MIN-MAX)

MPV (EDTA) and MPV citrate , both have been proved to have a statistically significant correlation with ischemic stroke with a p value < 0.001. The average MPV in cases was found to be 8.35±0.98 (EDTA) and 7.93±0.99 (citrate). The average MPV in controls was found to be 7.81±0.79(EDTA) and 7.30±0.74.

CHART 9 : COMPARISON OF MPV IN CASES AND CONTROLS



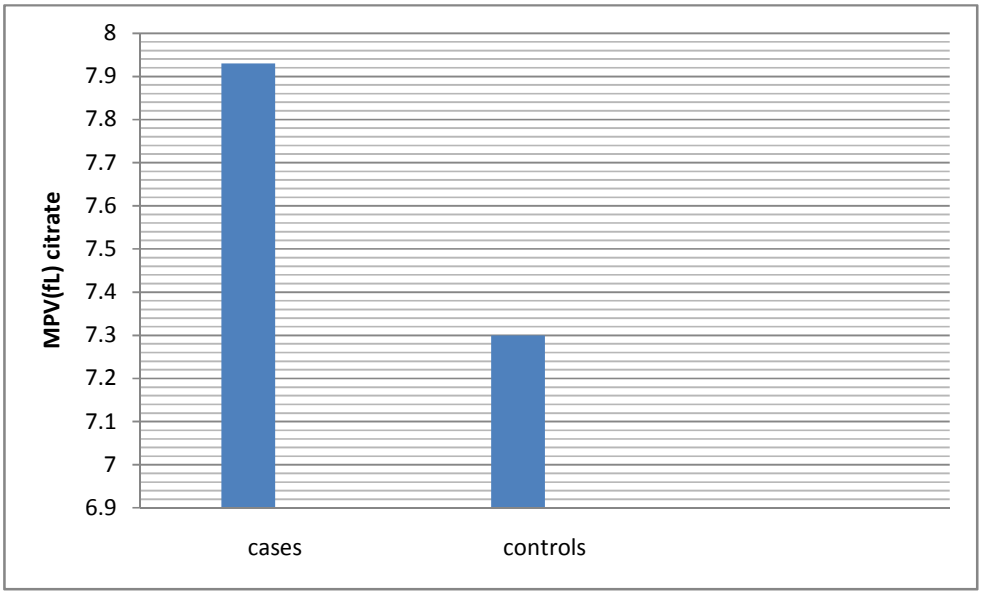


TABLE 13:THE OXFORDSHIRE COMMUNITY STROKE PROJECT CLASSIFICATION OF STROKE SYNDROMES AND CORRELATION WITH MPV

There was no statistically significant difference in MPV in each of the clinical subtypes of stroke.

STROKE SUBTYPE	NUMBER (n=100)	MPV (EDTA)	MPV(CITRATE)
LACS	66	8.29±0.94	7.87±0.93
POCS	24	8.59±0.98	8.17±1.07
PACS	8	8.21±1.28	7.81±1.29
TACS	2	7.9±1.27	7.4±0.85
SIGNIFICANCE		F=0.745 P=0.528	F=0.793 P=0.501

CHART 10 :THE OXFORDSHIRE COMMUNITY STROKE PROJECT CLASSIFICATION OF STROKE SYNDROMES AND CORRELATION WITH MPV (EDTA)

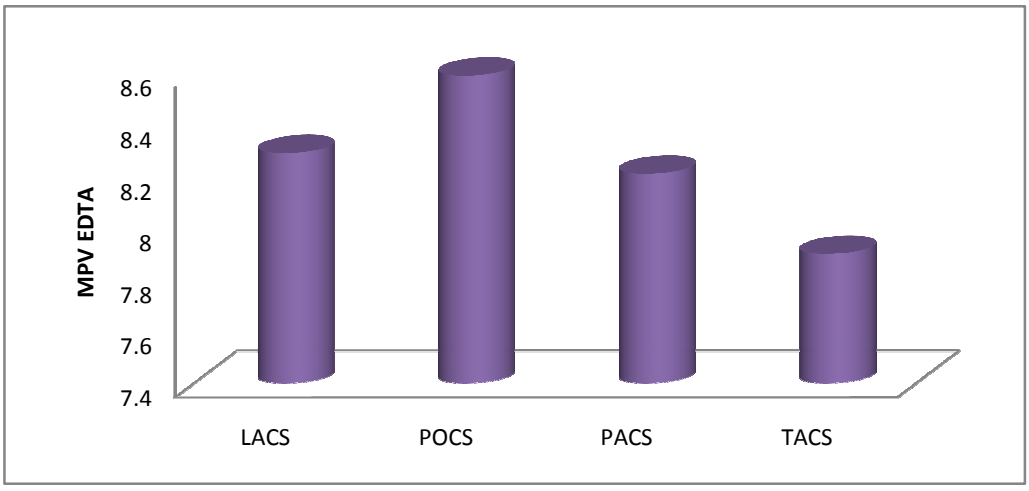


CHART 11:THE OXFORDSHIRE COMMUNITY STROKE PROJECT CLASSIFICATION OF STROKE SYNDROMES AND CORRELATION WITH MPV (CITRATE)

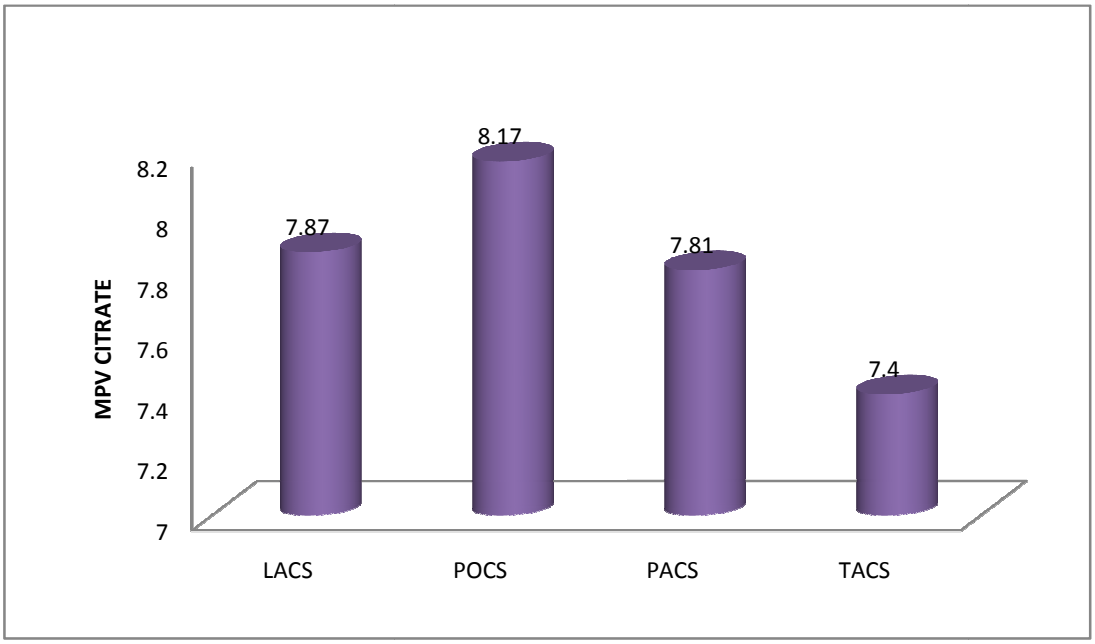


TABLE :14 CORRELATION BETWEEN PLATELET COUNT AND STROKE SUBTYPES

Stroke subtype	number	Platelet count
LACS	66	281212±127741
POCS	24	257375±127121
PACS	8	273875±98481
TACS	2	288000±45254
significance	F=0.220 P=0.882	

There is no statistically significant correlation between platelet count and stroke subtype

CHART 12 : CORRELATION BETWEEN PLATELET COUNT AND STROKE SUBTYPES

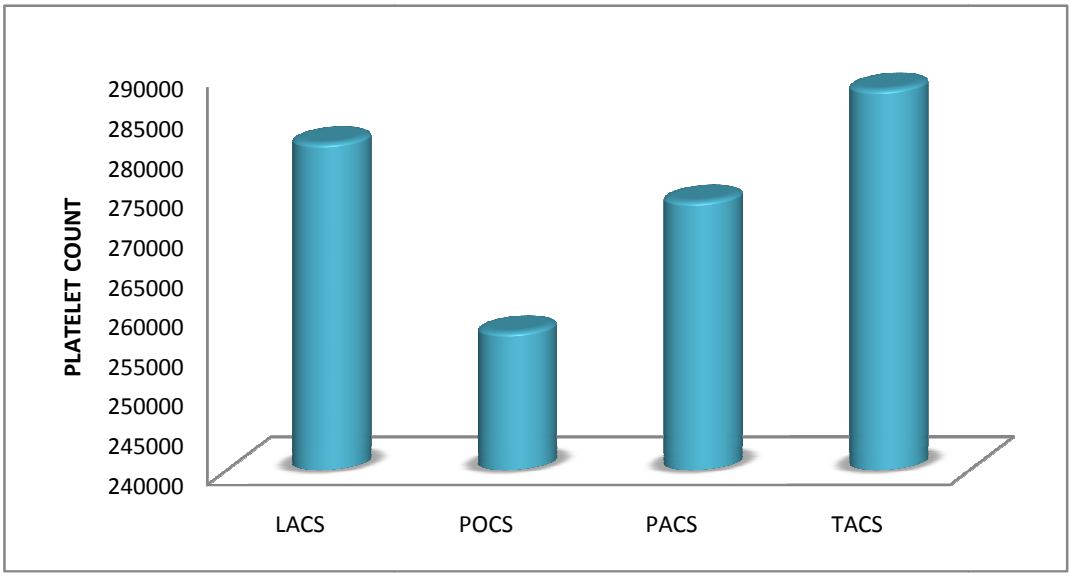


TABLE 15:CORRELATION BETWEEN STROKE –SEVERITY AND MPV

The association between MPV and severity of stroke was studied by comparing NIHSS with corresponding mean values of MPV in each group. No statistically significant correlation was seen.

NIHSS SCORE	NUMBER N=100	MPV (EDTA)	MPV(CITRATE)
1-4	3	7.6±0.2	7.07±0.21
5-15	29	8.29±0.92	7.9±0.94
16-20	21	8.37±0.89	7.9±0.94
21-42	47	8.43±1.08	8.01±1.06
SIGNIFICANCE	P VALUE	0.952	0.975

6.DISCUSSION

Previous studies have documented various platelet abnormalities in cerebrovascular diseases eg: circulating platelet aggregates, platelet aggregation, and increased release of platelet specific αgranule proteins, thereby indicating platelet activation. Others have shown that platelet aggregation is not increased in the acute phase but occurs several days after the event. This lack of detectable activation in the acute phase has been attributed to platelet consumption during the event. However, the lack of agreement between these studies may relate to specimen handling and different methodology.

6.1 DEMOGRAPHIC DATA

The study was a prospective study carried out from December 2013 to may 2014 at Coimbatore Medical College Hospital. 472 patients of stroke admitted to the medical wards were screened to get 100 cases. 372 cases of stroke were excluded . Delay in presenting to the hospital (i.e 48 hours after the onset of the symptoms as included in the exclusion criteria) comprised of 46.2% of the total exclusion. Haemorrhagic stroke (16.1%), delay in recruiting (16.7%), absence of an informed consent (15.1%) and platelet aggregates on peripheral smear (5.9%) were other causes of exclusion.

The mean age for the cases was 57.08±13.31 when compared to 57.21±13.23 for the controls. The maximum number of cases in the study were in the age group between 51 and 60. This was followed by the age group 61-70.

The average age for the males was 55.62±12.74 when compared to 55.85±12.60 in the controls. Females in the study population were older. Cases and controls comprised of 74% males and 26% females.

Table 16

COMPARISON OF THE DEMOGRAPHIC DATA OF THE CURRENT STUDY WITH THAT OF THE WESTERN LITERATURE

STUDY	O'Malley et al	Butterworth et al	Bath et al	Pikija et al	A.Muscari et al	Current study
No of cases Recruited	58	137	301	81	137	100
Demographics						
AGE,Y, MEAN±SD	79.5±6.5	71.9±10.8	65±9	76	78	57.08±13.31
WOMEN	39(67%)	55(40%)	87(29%)	49(60.5%)	65(47.4%)	26(26%)
MEN	19(33%)	82(60%)	214(71%)	32(39.5%)	72(52.6%)	74(74%)

Thus the mean age in our study was much lower than other studies. There is a clear male preponderance in the cases recruited in this study. Other studies also had a similar pattern except for the studies conducted by O'Malley et al and Pikija et al , where a female preponderance was seen.

6.2 RISK FACTORS FOR STROKE

Out of the many risk factors for stroke, hypertension was the most prevalent in the study group with a prevalence of 53%. Dyslipidemia came second with a prevalence of 33%. Diabetes mellitus came third with a

prevalence of 29%. Similar trend was seen in the other studies as mentioned below with hypertension being the most prevalent risk factor(84.7% in A.Muscari et al and 82.7% in Pikija et al). When compared to western studies, the representation of previous strokes as a risk factor was only 4%. Bath et al had 72% of previous strokes as this study was a substudy in which the benefits of ACE inhibitors (perindopril) in preventing a restroke was studied. Diabetes mellitus had a representation of 29% of cases which was higher than most of the western studies.

Table 17 COMPARISON OF RISK FACTOR PROFILE OF CURRENT STUDY WITH WESTERN LITERATURE

Study	O'Malley et al	Butterworth et al	Bath et al	Pikija et al	A.Muscari et al	Current study
No of cases recruited	58	137	301	81	137	100
RISK FACTORS						
Previous stroke/TIA	19(33%)	-	217(72%)	23(28.4%)		4(4%)
Hypertension	17(29%)	-	-	67(82.7%)	116(84.7%)	33(33%)
Atrial fibrillation	15(26%)	-	-	26(32.1%)	44(32.1%)	-
Previous MI	15(26%)	-	24(8%)	3(3.70%)	17(12.4%)	4(4%)
Angina pectoris	16(28%)	-	-	-	-	5(5%)
Alcohol	10(17%)	-	-	-	-	28(28%)
Peripheral vascular disease	7(12%)	-	-	2(2.47%)	-	-
Smoking	8(14%)	-	60(20%)	4(4.9%)	20(14.6%)	25(25%)

Diabetes mellitus	5(8.6%)	-	39(13%)	15(18.5%)	29(21.2%)	29(29%)

6.3 DRUG HISTORY

Table 18 :COMPARISON OF DRUG HISTORY OF PATIENTS IN THE CURRENT STUDY WITH WESTERN LITERATURE

STUDY	O'Malley et al	Butterworth et al	Bath et al	Pikija et al	A.Muscari et al	Current study
No of cases recruited	58	137	301	81	137	100
Drug history						
antiplatelets	19(33%)	-	211(70%)	33(40.7%)	59(43.1%)	-
Bblockers	3(5%)	-	-	-	-	10(10%)
Diuretics	24(41%)	-	-	-	-	6(6%)
Nitrates	7(12%)	-	-	-	-	3(3%)
Digoxin	11(19%)	-	-	-	-	1(1%)
Calcium antagonist	4(6.8%)	-	-	-	-	16(16%)
Statins			-	6(7.4%)	-	8(8%)
anticoagulants			-	2(2.5%)	-	-

Eventhough there were a few cases who had prior coronary artery disease or strokes, none of the stroke patients recruited were on antiplatelet drugs,as it was one of the exclusion criteria. This was included as an exclusion criteria because of the concern regarding the fact that concurrent usage of antiplatelets might influence the MPV studied. There has been previous studies with aspirin and

MPV and it showed no interference in vitro or in vivo. But there are other studies which have disproved this.

In this study,cases used predominantly antihypertensives with 16% of the hypertensives with 16% of the hypertensives on calcium antagonists followed by β blockers and diuretics.

6.4 PLATELET PARAMETES AND STROKE

Table 19:Comparison of platelet parameters of the current study with western literature

Study	Mean platelet volume(EDTA),fL	Mean platelet volume(citrate),fL	Platelet count, $x10^9$/L
O'Malley et al	11.3±0.85(11.3±0.85)		255±88 (299±80)
Butterworth et al	8.04±1.04(7.69±0.83)	7.35±1.05(7.09±0.74)	231±82(236±54)
Bath et al	10.0±2.1		233±80
Pikija et al	9.09(7.05-17.60)		197(106-637)
A.Muscari et al	8.21±1.04		244.1±86.7
Tohji et al	9.80±0.79 (10.72±0.63)		194±54(247±59
Current study	7.86±0.82 (7.58±0.70)		275±123(298±123)

6.5. STROKE SUBTYPES AND MPV

The Oxfordshire Community Stroke Project classification of stroke syndromes was used to classify strokes into Lacunar and Non lacunar syndromes (PACS,POCS,TACS). Two studies done by Butterworth et al and A.Muscari et al have shown statistically significant increase in MPV in non lacunar strokes as compared to lacunar strokes. Study done by O'Malley et al did not find out any such correlation. Also, in this study no statistically significant correlation was found out. This study concludes that patients with ischaemic stroke have larger platelets , a finding compatible with other reports of accentuated platelet function in brain infarction, including increased blood and urine levels of b-thromboglobulin (b-TG) and TxA2. However, it has not been possible to establish that thrombomegaly is restricted to patients with cortical ischaemic stroke. Cortical events are usually related to atherothromboembolic events that occur in the heart, aorta, carotid arteries or large intracranial arteries, and are likely to involve platelet activation. Conversely, many deep white matter lacunar strokes are considered to be a consequence of small vessel lipohyalinosis, a disease process not involving platelets[46].

6.6. STROKE SEVERITY AND MPV

The clinical severity of stroke at presentation was assessed using the National Institutes of Health Stroke scale and severe type of stroke was seen in 47% of cases with a score ranging from 21 to 42. 3% had only minor stroke with a score of 1-4, 29% had moderate stroke with a score ranging from 5 to 15, 21% had moderate to severe stroke with a score ranging between 16 and 20. The association of MPV with severity of stroke was determined by comparing the NIHSS score with the corresponding mean values of MPV in each group. MPV- EDTA showed a p value of 0.952 and MPV citrate showed a p value of 0.975, both of which were statistically insignificant. O'Malley conducted similar studies and assessed stroke severity using the modified Rankin's scale. In that study outcomes were divided as independent (Rankin's grade 0-2), dependent (Rankin's grade 3 to 5), and dead (Rankin's grade 6). However, no statistically significant correlation with MPV was obtained. Butterworth et al studied patients who were dead or dependent at 3 months, using the Lindley score, and they had a higher platelet volume , and a tendency to a lower platelet count as compared to those who fared well. But statistical significance was not obtained.

There is indirect evidence that the changes in MPV and platelet count are likely to have preceded the vascular event and are unlikely to be due to platelet consumption at the infarct site. Because the average life span of platelets is

about 8 days, the elevated MPV seen within the first 48 hours after stroke probably represent the platelets released before the infarction.

Also, it is unlikely that platelet consumption due to localized thrombosis would affect peripheral venous estimation of platelet variables. The observation that there was no difference in MPV between large cortical strokes and smaller lacunar infarctions also lends support to this view. Large platelets may promote the thrombotic event in a susceptible individual,and the increase in MPV may have contributed to the development of stroke rather than simply being a consequence of the acute event itself. In conclusion , this study has shown an increase in MPV and reduction of platelet count in acute stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required to know more about the role of platelet volume in stroke pathology, outcome, and most importantly , in individuals at risk for stroke.

6.7. LIMITATIONS OF THE STUDY

There are a few limitations to this study that needs to be mentioned.

1. 1.There were only 100 patients and controls in the study. Sample size was adequate , but was smaller than many of the western studies.

2. 2.There was no follow up done of the cases due to time constraint. If on follow up a persistent increase of MPV was demonstrated, it would have given more strength to the hypothesis that the increase in MPV may have contributed to the development of stroke rather than simply being a consequence of the acute event itself.
3. Seriously ill patients directly admitted to the intensive care unit have not been included in the study due to difficulty in getting consent. This could have led to selection bias. This would have reflected upon the correlation of MPV and severity of stroke.
4. The controls have been matched for age, sex ,and most of the risk factors like hypertension, diabetes mellitus, alcoholism and dyslipidemia. Other risk factors like smoking, coronary artery disease, and previous strokes could not be perfectly matched, which would have been ideal. But, most of the western studies have also been carried out on only age and sex matched controls.

SUMMARY

Cerebrovascular diseases include some of the most devastating and common neurological disorders. They cause approximately 200,000 deaths per year in the United States and are a major cause of morbidity. The prevalence of stroke in India was estimated as 203 per 100,000 population above 20 years, amounting to a total of about 1 million cases. It was found to be the sixth leading cause of disability adjusted life years (DALY; one DALY is one lost year of healthy life) in 1990 and is projected to rank four by the year 2020[13].

Platelets play a major role in the pathogenesis of vascular disease , and the mean platelet volume is a physiological variable of hemostatic importance. Larger platelets are more reactive, produce more prothrombotic factors [3 and 4], and aggregate more easily. They also have more of dense granules and also release more of serotonin and β thromboglobulin than smaller platelets. Platelets lack a nucleus and their characteristics are determined by their progenitor cells, the bone marrow megakaryocytes. Ischaemic stroke is thought to occur as a result of thrombotic occlusion of a stenosed atherosclerotic blood vessel. Initially platelets adhere to the damaged vessel , resulting in the recruitment of further platelets, followed by aggregation,platelet plug formation and finally, thrombotic occlusion. So the detection of large platelets in patients would lend

support to the idea that platelet volume influences thrombotic large vessel occlusion leading to ischaemic stroke.

Though there are quite a few studies indicating the association of platelet volume with myocardial infarction, only a very few studies have been conducted to find out the correlation between platelet size and ischaemic stroke. Also , among these studies, there have been discrepancy regarding sample size, the methodology used and the final results. There are no well documented studies in India comparing the association of mean platelet volume with ischaemic strokes. This was a prospective study and data was collected from December 2013 till May 2014, at Coimbatore Medical college hospital, Coimbatore , a tertiary care referral centre. The study was carried out among 100 patients diagnosed to have an acute ischaemic stroke and admitted to the medical wards in the hospital within 48 hours of onset of symptoms as well as satisfying the inclusion and exclusion criteria. The data was compared with 100 controls matched for age, sex ,as well as known risk factors for stroke like diabetes mellitus, hypertension, dyslipidemia, smoking and alcoholism.

Key findings included:

1) The main parameter studied was MPV. MPV has got a statistically significant correlation with ischaemic stroke with a p value less than 0.001. this was true for both EDTA as well as citrate samples. The average MPV in cases was 8.35±0.98 (EDTA) and 7.93±0.99 (citrate). The average MPV in controls being 7.81±0.79 (EDTA) and 7.30±0.74 (citrate). Therefore, the study shows an elevated MPV in the acute phase of ischaemic stroke. Within this relationship and confounding for other significant variables in the multivariate regression analysis, it can be stated that an increase in MPV is independently associated with stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and likely to represent changes occurring at the time of thrombopoiesis. Further research is required to enquire about the role of platelet volume in stroke pathology, outcome, and more importantly, in patients at risk for stroke.
2) The platelet count in patients with stroke is lower with average being 275±123 (100-5,44) compared to controls with an average of 299±124(100-518).
3) The Oxfordshire Community stroke project classification of stroke syndromes was used to classify strokes into Lacunar and Nonlacunar syndromes (POCS, PACS, TACS).The association of MPV with stroke

subtype was assessed by comparing the stroke subtype with corresponding mean values of MPV's in each group.MPV EDTA showed a p value of 0.523 and citrate 0.511, both of which were statistically insignificant. Therefore, In this study, no statistically significant correlation was established between MPV and stroke subtypes.

4) The clinical severity of stroke at presentation was determined using the National Institutes of health Stroke scale and severe stroke was seen with 47% of cases. 3% had only minor stroke.29 % had moderate severity stroke and21 % had moderate to severe stroke. The association of MPV with severity of stroke was determined by comparing the NIHSS with corresponding mean values of MPV's in each group. MPV EDTA showed a p value of 0.952 and MPV citrate showed a p value of 0.975, both of which were statistically insignificant.

In conclusion, this study has shown an elevation of MPV and a reduction of platelet count in acute stroke. With this relationship and confounding for other significant variables, an increase in MPV is independently associated with stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required to enquire into the role of platelet volume in stroke pathogenesis, outcome, and more importantly in individuals at risk for stroke.

7. CONCLUSIONS

1. This study has shown an elevation of MPV in acute phase of ischaemic stroke. Within this relationship and adjusting for other significant variables in multivariate regression analysis, it can be stated that an increase in mean platelet volume is independently associated with stroke. The observations here suggest a role for larger platelets in the genesis of cerebral thrombosis and are likely to represent changes occurring at thrombopoiesis. Further research is required into the role of platelet volume in stroke pathology, outcome, and most importantly, in individuals at risk for stroke.

2. This study did not find a statistically significant correlation between clinical severity of stroke and mean platelet volume.

3. This study showed no statistically significant correlation between mean platelet volume and stroke subtypes. Thrombomegaly is restricted not just to patients with cortical ischemic stroke but is also seen with lacunar syndromes.

BIBLIOGRAPHY

1) O'Malley T, Langhorne P, Elton R,Stewart C. Platelet size in stroke patients. Stroke 1995;26:995-999.

2) Pathansali R, Smith N M,Bath P M. Prothrombotic megakaryocyte and platelet changes in hypertension are reversed following treatment: pilot study.Blood2001;12:144-149.

3) Ross R.Cell biology of atherosclerosis.Annual review of physiology 1995;57:791-804.

4) Bath P, Algert C, Chapman N,Neal B. Association of mean platelet volume with risk of stroke among 3134 individuals with history of cerebrovascular disease. Stroke 2004;35:622-626.

5) D'Erasmo, Aliberti G,Celi F. platelet count, mean platelet volume and their relation to prognosis in cerebral infarction. Journal of internal medicine 1990,227:11-14.

6) Tohgi H, Suzuki H, Tamura K,et al. Platelet volume,aggregation and adenosine triphosphate release in cerebral thrombosis. Stroke 1991;22:17-21.

7) Smith N, Panthansali R,Bath P. Platelets and stroke. Vascular medicine1999;4:165-172.

8) Bath PMWButterworth R J. platelet size: measurement, physiology and vascular disease. Blood 1996;7;157-161.

9) Thomson CB,Love DG, Quinn P G,Valeri C R. Platelet size does not correlate with platelet age. Blood. 1983;62:487-494.

10) Smith W S,English J D,Johnson SC. Cerebrovascular diseases. Harrison's principle of internal medicine.Ed. Fauci AS,Braunwald E,Kasper DL,Hauser SL, Longo DL,Jameson JL etal 17th edition.Mc Graw Hill; volue 2;2513-2535.

11) Victor M, Ropper AH, Adams RD. cerebrovascular disease.Adam's and Victor's principles of neurology.Ed.RopperA H,Samuels M A,. 9th ed. United states of America, Mc Graw Hill2009.

12) Cordonnier C, leys D. Stroke the bare essentials. Neurology in practice 2008;8:263-272.

13) P k Sethi. Stroke-Incidence in India and management of ischaemic stroke. Neurosciences Today; VolVI no 3.July-september. 2002.

14) Greisenegger S,Endler G,Hsieh K,Tentschert,MannhalterC,Lalouschek W. Is elevated mean platelet volume associated with a worse outcome in patients with acute ischemic cerebrovascular event? Stroke2004;35:1688-1691.

15) History of stroke. www.healthsystem.virginia.edu,28/9/2009.

16) Harrison P, Watson SP. The vascular function of platelets. Postgraduate haematology.Ed.HoffbrandAV, Catovsky D, TuddenhamEGD.5th edition New Delhi, Blackwell publishers;2005;808-824.

17) Buckley MF, James J W,Brown D E,Whyte G S, Dean MG, Chesterman CN, et al.A novel approach to the assessment of variations in the human platelet count. Thromb Haemost2000;83:480-84

18) George JN.Platelet IgG: measurement, interpretation, and clinical significance. Prog Hemost Thromb.1991;10:97-126.

19) Paulus JM.platelet size in man. Blood 1975;46:321-326 9abstract).

20) Frojmovic MM,Panjwani R.Geometry of normal mammalian platelets by quantitative microscopic studies.Biophys J 1976;16:1071-89(abstract).

21) White JG. Electron microscopic studies of platelet secretion. Prog Hemost Thromb1974;2:49-98.

22) White JG,ClawsonGC. Overview article: biostructure of blood platelets. Ultrastruct pathol 1980;1:533-558.(Abstract)

23) White JG. Anatomy and structural organization of the platelet. Haemostasis and thrombosis.Basic principles and clinical practice.Ed Colman RW, Hirsh J, Marder VJ,Salzman EW,eds,2nd edition, Philadelphia: J B Lippincott Co;19871;537-554.

24) Chevalier J,Nurden A T, Thiery J M. freeze fracture studies on the plasma membranes of normal human,thrombasthenic and Bernard Soulier platelets.J lab Clin med1979;94:232-245.

25) Behnke O. an electron microscopic study of the megakaryocyte of the rat bone marrow. The developmentof the demarcation membrane

system and the platelet surface coat.J Ultrastruct Res 1977;61:201-214.(abstract)

26) Handagama P,Shuman M A,Bainton DE. Incorporation of intravenously injected albumin, immunoglobulin G,and fibrinogen in guinea pig megakaryocyte granules.J Clin Invest 1989;84:73-82.(Abstract).

27) Radley JM,Haller CJ. Fate of senescent megakaryocytes in the bone marrow. Br J Haematol 1983;53:277-287

28) Sixma JJ, Wester J.The hemostatic plug. Semin hematol1977;14:265-299.(abstract)

29) Grottum KA,Solum NO. congenital thrombocytopenia with giant platelets: a defect in the platelet membrane. Br J hamatol 1968;16:277-285.

30) Coller BS. Biochemical and electrostatic considerations in primary platelet aggregation. Ann NY Acd Sci1984;416:693-704. (abstract)

31) White J G. Is the canalicular system the equivalent of the muscle sarcoplasmic reticulum? Hemostasis 1975;4:185-191(abstract)

32) Fox JEB.platelet cytoskeleton. Thrombosis and haemostasis. Basic principles and clinical practice.Ed. Colman RW, Hirsh J, Marder VJ,et al.4th ed.Philadelphia, Lippincott Williams and Wilkins:2001 ;429-446.

33) Cramer EM. Platelets and megakaryocytes: anatomy and structural organization. Thrombosis and hemostasis. . Basic principles and clinical

practice.Ed. Colman RW, Hirsh J, Marder VJ,et al.4th ed.Philadelphia, Lippincott Williams and Wilkins:2001 ;411-428.

34) FukamiMH,Holsmen H, Kowalska A. platelet secretion .Ed. Colman RW, Hirsh J, Marder VJ,et al.4th ed.Philadelphia, Lippincott Williams and Wilkins:2001 ;561-573.

35) Holsmen H, Kaplan K L,Dangelmeir CA. differential energy requirements for platelet responses: a simultaneous study of aggregation. Biochem J1984;208:9-21

36) VerhoevenAJM, Mommer steeg ME, AkkermanJWN. Biochem J1984;221:777-786

37) Zarbock A.Platelet neutrophil interactions: linking hemostasis and inflammation. Blood Rev2007;21:99

38) De Duve C. biochemical studies on occurrence,biogenesis, and life history of mammalian peroxisomes. J Histochem ytochem1973;21:941-48 (abstract)

39) Van den BH de Vet EC,Zomer AS. The role of peroxisomes in ether lipid synthesis.Adv exp Med Biol 1996;416;33-41.(abstract)

40) Morgenstern E. coated membranes in blood platelets. Eur J cell Biol 1982;26:315-318.

41) Akkerman JWN,Gorter G,Holmsen HBiochem Biophys Acta 1983;760:34-42

42) Holmsen H,Farstad M. Energy metabolism.In: platelet responsers and metabolism.vol 21987;245-282 9abstract)

43) Harrison P, Watson SP. Post graduate hematology.Ed. Hoffbrand AV,Catovsky D, Edward G. 5th ed. New Delhi. Blackwell publishers;2005;808-824

44) Kaito K, Otsubo H, Usui N et al. Br J hematol 2005;128:698-702

45) Muscari A, Puddu GM. Thromb Res2008

46) Butterworth RJ,Bath PMW.the relationship between mean platelet volume, stroke subtype and clinical outcome.platelets 1998;9:359-364

47) Pikija S, Hajduk M. clinical neurology and neurosurgery 2009;111: 568-73

48) Erhart s,Beer JH,Reinhart WH. Acta hematol1999;101:140-144

49) Butkiewicz AM,Kemona H,Lipska A.Thrombosis research2006;118:199-204. (abstract)

50) Coban E, Berkant AA.The mean platelet volume inpatients with essential and white coat hypertension. Platelets.2005;16:435-438

51) Zuberi BF,Akhtar N,Afsar S. Singapore Med J original article2008;49:114

52) Lippi G, Salvagno GL,Guidi GC.Relationship between mean platelet volume and biochemical parameters of metabolic syndrome. Clin drug Invest 2007;27:731-732

53) Butkeiwicz AM,Kemona, Radziwon P. advances in medical sciences2006;51:111-120

54) Khandekar MM, Khurana AS,Deshmukh SD. Platelet volume indices in patients with coronary artery disease and acute myocardial infarction;J Clin Pathol2006;59:146-149

55) Rankin J,cerebral vascular accidents in patients over the age of60. Scott med J1957;2:200-215

56) Bonita R modification of Rankin Scale: recovery of motor function after stroke; Stroke 1988;19: 1497-1500

57) de KoningL Merchant AT. European heart J 2007;28:850 -856

58) Gupta R, Rastogi P,Sarna M Gupta VP.JAPI 2007;55:621-627

59) DagenaisGR, Yi Q, Mann JFE, Bosch J.Am heart J2005;149:54-60

60) Rosner B. Fundamentals of biostatistics. 5th edition, Duxbury,2000;11:80-240

61) Reddy MV. Statistics for mental health care research, NIMHANS publications2002;12:108-144

62) Rao PS ,Richard J. an introduction to biostatistics;86-160

63) Griner PF,Mushlin AI, Greenland P.Annals of internal medicine;1981;94:555-600.

64) Patel SR, Hartwig JH,Italiano JE Jr. the biogenesis of platelets from megakaryocyte proplatelets. The journal of clinical investigation 2005;115;3348-3354

65) Harold P Adams, John W Norris. Ischemic cerebrovascular disease, CNS series 2003; 1-46

66) Feigin VL, Wiebers DO, Nikitin YP, O'Fallon WM, Whisnant JP. Risk factors for ischemic stroke in a Russian community : a population based casecontrol Study. Stroke 1998; 29: 34-39.

67) P.M. Dalal. Cerebrovascular Disorders, API Textbook of Medicine, 7th Edition, Association of Physician of India, 2003; 796-798.

68) Charles Warlow. Stroke, transient ischaemic attack and intracranial venous thrombosis : Brain's Disease of the nervous system.11th edition, Oxford University Press, 2001; 776-830.

69) Wade S Smith, S. Claiborn Johnston, J. Donald Easton. Cerebrovascular Disease, Harrison's Principles of Internal Medicine 16th Edition, McGraw Hill Medical Publications, 2005; 2372-2387.

70) Ronald L Eisenberg. Radiology – An Illustrated History, Mosby year book, 1992; 467-473

PROFORMA FOR CASES

A STUDY ON THE ASSOCIATION OF MEAN PLATELET VOLUME WITH ISCHAEMIC STROKE AND ITS CORRELATION WITH STROKE SUBTYPES

Case no:

Name : I.P. No. :

Age : Date of

Admission:

Sex : Date of

Discharge :

Occupation : Unit:

Address :

Complaints with duration :

History of Present illness :

1. Weakness of limbs : Present/ Absent

If present

a. Limbs involved : Upper limb : Right / left Lower limb : Right / Left

b. Mode of onset : Sudden / Insidious / Slow

c. Duration : d. Progression :

2. Weakness of Face : Present / Absent

If present :

a. Part of face involved : Upper / Lower

b. Deviation of angle of mouth : Right side / Left side

c. Difficulty in closing eyes : Present / Absent

3. Level of Consciousness Alert / Drowsy / Unconscious

4. Speech disturbances : Present / Absent

If present :

a. Slurring of speech : Present / Absent

b. Comprehension : Normal / Abnormal

5. History suggestive of Cranial nerve palsy ;

H/o Blurring of Vision : Present / Absent

Diplopia : Present / Absent

Dysphagia : Present / Absent

Nasal regurgitation : Present / Absent

6.H/o Sensory disturbances : Present / Absent

PAST HISTORY

1. History of previous cerebrovascular accidents : Yes / No

2. History of TIA : Yes / No

3. History of IHD : Yes / No

4. History of Hypertension : Yes / No

5. History of diabetes mellitus : Yes / No

6. History of RHD : Yes / No

Personal History :

Smoking : Yes / No

Alcohol intake : Yes / No

Drug history: antiplatelets, antihypertensives, chemotherapy drugs

GENERAL PHYSICAL EXAMINATION :

Vital signs: Pulse : B.P. : R/R :

NS examination – NIHSS assessment

CVS examination

Respiratory system examination

Per abdomen examination

INVESTIGATION :

Platelet count

Mean platelet volume

Peripheral smear

Lipid profile

Blood Glucose : FBS PPBS

ECG

C.T. SCAN

NIHSS score

PROFORMA FOR CONTROLS

Name : I.P. No. :

Age : Date of Admission:

Sex : Date of Discharge :

Occupation : Unit:

Address :

PAST HISTORY

1. History of previous cerebrovascular accidents : Yes / No

2. History of TIA : Yes / No

3. History of IHD : Yes / No

4. History of Hypertension : Yes / No

5. History of diabetes mellitus : Yes / No

6. History of RHD : Yes / No

Personal History :

Smoking : Yes / No

Alcohol intake : Yes / No

Drug history: antiplatelets, antihypertensives, chemotherapy drug

INVESTIGATION :

Platelet count

Mean platelet volume

Peripheral smear

Lipid profile

Blood Glucose : FBS PPBS

ECG

CONSENT FORM(CASES)

Mr/Mrs/Ms……,

…….(relationship) of……(legal guardian) is being asked to be a participant in the research study titled "" A STUDY ON THE ASSOCIATION OF MEAN PLATELET VOLUME WITH ISCHAEMIC STROKE AND ITS CORRELATION WITH STROKE SUBTYPES "" in CMC Hospital, Coimbatore, conducted by Dr.V.BHAVANA, Post Graduate Student in the Department of General Medicine, Coimbatore Medical College. He /she satisfies eligibility as per the inclusion criteria. You/legal guardian can ask any question you may have before agreeing to participate.

Research Being Done

A STUDY ON THE ASSOCIATION OF MEAN PLATELET VOLUME WITH ISCHAEMIC STROKE AND ITS CORRELATION WITH STROKE SUBTYPES

Purpose of Research

Aim of the study is to find out the correlation between mean platelet volume and ischaemic stroke and to find out whether there is any correlation between mean platelet volume and stroke subtype as well as between stroke severity and mean platelet volume.

It includes details like age,sex and history of diabetes, hypertension ,coronary artery disease, smoking and alcoholism

Investigations includes platelet count, peripheral smear, mean platelet volume, blood sugar, lipid profile , electrocardiogram & CT scan Brain

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

Statement of Consent

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

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Signature /Left thumb impression (volunteer) **Date**

---------- ----------

Signature of witness **Date**

CONSENT FORM(CONTROLS)

Mr/Mrs/Ms……,
…….(relationship) of……(legal guardian) is being asked to be a participant in the research study titled "" A STUDY ON THE ASSOCIATION OF MEAN PLATELET VOLUME WITH ISCHAEMIC STROKE AND ITS CORRELATION WITH STROKE SUBTYPES " in CMC Hospital, Coimbatore, conducted by Dr.V.BHAVANA, Post Graduate Student in the Department of General Medicine, Coimbatore Medical College. He /she satisfies eligibility as per the inclusion criteria. You/legal guardian can ask any question you may have before agreeing to participate.

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Signature /Left thumb impression (volunteer) **Date**

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Signature of witness **Date**

ஒப்புதல் படிவம்

பெயர் :

பாலினம் : வயது :

முகவரி :

அரசு கோவை மருத்துவக் கல்லூரியில் பொது மருத்துவத் துறையில் பட்ட மேற்படிப்பு பயிலும் மாணவி மேற்கொள்ளும் **"இரத்த உணர்வு செல்லின் அளவு மற்றும் பக்கவாத நோயிக்கும் இடையே உள்ள சம்மந்தத்தை அறிதல் என்ற தலைப்பில்"** குறித்த ஆய்வில் செய்முறை மற்றும் அனைத்து விவரங்களையும் கேட்டுக் கொண்டு எனது சந்தேகங்களை தெளிவுப்படுத்திக் கொண்டேன் என்பதை தெரிவித்துக் கொள்கிறேன்.

நான் இந்த ஆய்வில் முழு சம்மதத்துடனும், சுய சிந்தனையுடனும் கலந்து கொள்ள சம்மதிக்கிறேன்.

இந்த ஆய்வில் என்னுடைய அனைத்து விபரங்கள் பாதுகாக்கப்படுவதுடன் இதன் முடிவுகள் ஆய்விதழில் வெளியிடப்படுவதில் ஆட்சேபனை இல்லை என்பதை தெரிவித்துக் கொள்கிறேன். எந்த நேரத்திலும் இந்த ஆய்விலிருந்து நான் விலகிக் கொள்ள எனக்கு உரிமை உண்டு என்பதையும் அறிவேன்.

இடம் : கையொப்பம் / ரேகை

நாள் :

MASTER CHART - CASES

Sl.No	Name	Age	Sex	Risk factors							Clinical profile	Stroke subtype	NIHSS	PLT	MPV	
				DM	HTN	D	S	A	CAD	Stroke					EDTA	Citrate
1	MURUGAN	31	M				P	P			FP, Motor	LACS	17 mod-severe	1,00	8.3	7.8
2	DURAI	33	M		p						FP, Motor	LACS	37 severe	150	7.3	7
3	SAMPATH	43	M		p		p				cerebellar	POCS	18 mod-severe	300	8.6	8.2
4	MUNIYAN	48	M		p		p	p			hemi,FP,HH,Aphasia	TACS	32 severe	256	8.8	8
5	PAPPATHI	57	F	p		p					motor,sensory	LACS	8 mod	320	9.8	9.4
6	AKBERUDDEEN	52	M	p	p						FP, Motor	POCS	5 mod	222	8	7.2
7	SHANMUGAM	55	M		p						FP, Motor	LACS	4 minor	122	7.4	6.9
8	ROSEN BEEVI	60	F		p						FP, Motor	LACS	18 mod-severe	256	7.8	7.6
9	GOVINDRAJ	55	M	p	p						cerebellar	POCS	22 severe	117	8.9	8.5
10	PALANISAMY	60	M	p	p						FP, Motor	POCS	12 mod	120	8.9	8.3
11	RAJU	55	M								FP, Motor	LACS	30 severe	123	7	6.5
12	KUMAR	60	M		p						motor,sensory	LACS	6 mod	145	7.8	7.6
13	DEVANAGAI	67	F		p	p		p			hemi,FP,HH,Aphasia	POCS	23Severe	236	9.4	9
14	PAUL RAJ	68	M		p					p	FP, Motor	LACS	17mod-severe	290	8.1	7.9

15	SENTHIL	63	M				p	p			FP, Motor	LACS	28 severe	389	9.5	9.1
16	MADHAN	64	M		p			p			FP, Motor	LACS	38 severe	106	7.4	7
17	SUBRAMANI	69	M		p	p					FP, Motor	LACS	25 severe	114	9.5	8.7
18	RAMASAMY	72	M				p				FP, Motor	LACS	20 mod-severe	180	8.8	8
19	KANNAMAL	77	F		p						hemi,FP,HH,Aphasia	TACS	35 severe	320	7	6.8
20	GOPAL	83	M	p							FP, Motor	LACS	29 severe	209	6.9	6.8
21	PAPPAMMAL	35	F			p					cerebellar	POCS	20 mod-severe	187	8.4	7.7
22	RAJA	39	M		p		p		p		motor,sensory	LACS	28 severe	176	7.5	7.3
23	TAMIL ARASU	44	M		p	p	p				motor,sensory	LACS	16 mod-severe	390	9.6	9.1
24	CHINNAMMAL	49	F		p						FP, Motor	LACS	26 severe	187	7.9	7.3
25	KUPPUSAMY	56	M		p		p				monoplegia	PACS	8 mod	389	9.4	9.2
26	SURESH	51	M	p				p			motor,sensory	LACS	31 severe	400	7	6.8
27	SHANTHI	56	F	p		p					FP, Motor	LACS	8 mod	500	7.8	7.5
28	MOHAMED	51	M		p			p			FP, Motor	POCS	7 mod	200	8.7	8.4
29	PRABHU	56	M		p	p	p				hemi,FP,HH,Aphasia	POCS	25 severe	310	9.8	9.6
30	SHANKAR	51	M		p			p			FP, Motor	LACS	18 mod-severe	215	7	6.3
31	RAMKUMAR	56	M		p	p		p			motor,sensory	LACS	35 severe	346	7.9	7.5

32	ANNADURAI	63	M					p			motor,sensory	LACS	8 mod	216	8.9	8.6
33	BALA SUNDARAM	68	M	p		p					monoplegia	PACS	17mod-severe	310	6.8	6.3
34	DHANALAKSHMI	67	F			p					cerebellar	POCS	18 mod-severe	387	8.8	8.2
35	PERIYASAMY	62	M		p	p		p			cerebellar	POCS	40 severe	540	6.6	6.1
36	RAJENDRAN	65	M		p			p			motor,sensory	LACS	36 severe	322	8	7.5
37	JOTHI	70	F		p						cerebellar	POCS	24 severe	322	9	8.8
38	RAJAMMAL	73	F								motor,sensory	LACS	22 severe	544	8.9	8.8
39	VENKATESH	78	M			p	p	p			monoplegia	PACS	12 mod	145	9.5	9.1
40	DEVAN	36	M	p		p					FP, Motor	LACS	40 severe	233	7.5	7
41	TAMIL SELVAN	32	M			p	p	p			FP, Motor	LACS	19 mod-severe	320	7.9	7.3
42	RAMALINGAM	45	M	p			p	p			motor,sensory	LACS	21severe	200	9.8	9.3
43	KUMARI	50	F			p					monoplegia	PACS	6mod	320	6.5	6.1
44	ERUSAN	55	M		p			p			motor,sensory	LACS	13 mod	210	8.7	8.3
45	PERIYAN	52	M		p	p		p			FP, Motor	LACS	33 severe	322	8	7.7
46	RAJESWARI	57	F	p							FP, Motor	LACS	10mod	432	8.4	8.3
47	RAJA	52	M		p						FP, Motor	LACS	10 mod	210	9.8	9.5
48	GOTHANDAM	57	M		p		p	p			FP, Motor	LACS	29 severe	322	6.4	6.1
49	SIVA	52	M				p				monoplegia	PACS	4 minor	106	7.8	7.3

50	LOGANATHAN	57	M	p		p			p		FP, Motor	POCS	26 severe	150	8.8	8.5
51	LAZER	64	M				p				FP, Motor	LACS	17 mod-severe	178	9.8	9.6
52	MARIMUTHU	69	M		p		p	p			FP, Motor	LACS	10 mod	288	6.6	6.4
53	JAMES	66	M	p							motor,sensory	LACS	22 severe	100	8.8	8.4
54	SIVALINGAM	61	M	p	p						motor,sensory	LACS	39 severe	207	8.8	8.5
55	SANTHANAM	66	M			p	p				hemi,FP,HH,Aphasia	POCS	35 severe	365	8.8	8.4
56	LAKSHMI	76	F								motor,sensory	LACS	23Severe	508	9.3	8.9
57	MANI	74	M		p	p	p		p		FP, Motor	POCS	5mod	100	7.4	7.1
58	PARVATHY	79	F	p							FP, Motor	POCS	20mod-severe	190	9.6	9.4
59	RANI	38	F		p	p					FP, Motor	LACS	38severe	367	7.6	7.1
60	MOHANNA	46	F		p	p					motor,sensory	LACS	22severe	540	10	9.6
61	ARUMUGAM	42	M		p						cerebellar	POCS	18 mod-severe	123	6.8	6.3
62	MANIKANDAN	54	M		p		p				motor,sensory	LACS	16 mod-severe	245	8.2	7.4
63	MARIYAPPAN	53	M		p	p			p		motor,sensory	LACS	35 severe	238	8.6	8.2
64	MANIKAM	58	M		p			p			motor,sensory	LACS	12 mod	190	9.6	9.4
65	RAJIV	53	M							p	FP, Motor	LACS	13 mod	289	7.5	7.1
66	BALAMURUGAN	58	M	p			p				FP, Motor	LACS	24 severe	489	8	7

67	RAMARAJ	53	M		p	p	p				FP, Motor	LACS	22 severe	287	8.6	8.3
68	THANGARAJ	58	M		p		p				FP, Motor	LACS	38 severe	156	9.8	9.5
69	SELVARAJ	65	M			p					cerebellar	POCS	18 mod-severe	288	7.8	7.7
70	MUTHURAJ	70	M		p						FP, Motor	LACS	13 mod	299	7.8	7.5
71	SHAJAHAN	65	M	p		p					FP, Motor	POCS	25 severe	478	8.5	8.6
72	KANDASAMY	62	M	p					p		FP, Motor	LACS	38 severe	389	8.6	7.9
73	RANGAN	67	M		p	p		p			FP, Motor	LACS	30 severe	229	9.8	9
74	GOMATHY	78	F	p							monoplegia	PACS	15 mod	346	8.5	8
75	KOKILAVANI	75	F		p				p		cerebellar	POCS	15 mod	209	7.3	6.4
76	PALANI	80	M		p						motor,sensory	LACS	25 severe	280	7.3	7
77	PALANIAPPAN	40	M		p	p					monoplegia	PACS	10 mod	308	7.4	7.2
78	GOWRI	42	F	p	p	p				p	FP, Motor	LACS	22 severe	416	8.5	8
79	MAHESWARI	47	F								cerebellar	POCS	30 severe	267	9.6	9.4
80	GANESH	44	M			p	p	p			motor,sensory	LACS	10 mod	370	8.8	8.1
81	SARAVANAN	53	M	p		p	p	p			FP, Motor	LACS	4 minor	408	7.6	7
82	ANTONY	54	M	p	p					p	FP, Motor	POCS	38 severe	166	9.8	9.3
83	MUNUSAMY	54	M	p		p			p		FP, Motor	LACS	15 mod	295	7.8	7.7
84	BASHEER	59	M		p	p		p			FP, Motor	LACS	32 severe	232	7.8	7.2
85	SELVAMANI	54	M	p							monoplegia	PACS	5 mod	267	9.8	9.3
86	SUDHA	59	F		p						cerebellar	POCS	39 severe	289	7.2	6.6

87	PONNUSAMY	66	M	p	p			p			FP, Motor	LACS	20 mod-severe	104	8.8	8.7
88	VELADURAI	69	M				p	p			FP, Motor	LACS	16 mod-severe	328	8.4	7.8
89	BANUMATHI	64	F		p						hemi,FP,HH,Aphasia	POCS	26 severe	507	9.9	9.2
90	THANGARAJ	63	M								FP, Motor	LACS	40 severe	378	10	9.4
91	MANIKAM	68	M	p							cerebellar	POCS	26 severe	104	9.6	9.3
92	RAMANI	71	F	p					p		FP, Motor	LACS	18 mod-severe	246	9.8	9.1
93	GANDIMATHI	76	F	p				p			FP, Motor	LACS	18 mod-severe	209	7.8	7.4
94	KAVITHA	82	F		p						FP, Motor	LACS	28 severe	489	6.5	6.2
95	RANGARAJ	28	M								FP, Motor	LACS	6 mod	326	7.8	7.3
96	VELUSAMY	27	M	p							FP, Motor	LACS	7 mod	389	8	7.5
97	ARIVALAGAN	24	M								FP, Motor	LACS	10 mod	489	7.9	7.4
98	AZHAGARASAN	26	M					p			FP, Motor	LACS	15 mod	165	8.2	7.6
99	MUTHULAKSHMI	41	F						p		FP, Motor	LACS	20 mod-severe	399	8.6	8.1
100	DURAISAMY	60	M		p	p					motor,sensory	LACS	6 mod	172	7.8	7.6
														117.2183		

MASTER CHART - CONTROLS

sl no	name	age	sex	risk factors							MPV EDTA	MPV citrate	PLT count
				DM	D	HTN	S	A	CAD	Stroke			
1	AROKIYASAMY	32	M				p				8	7.4	1,88,000
2	VELUSAMY	40	M		p	p		p			7	6.6	1,89,000
3	VELUMURUGAN	45	M	p			p				8.3	7.8	2,30,000
4	MURUGAN	43	M			p		p			7.6	7.6	3,08,000
5	SHANTHA	56	F			p				p	8.1	8.1	4,89,000
6	LINGAN	53	M		p	p					8.2	7.8	1,45,000
7	LOGANATHAN	57	M	p		p		p			7.1	6.5	3,99,000
8	MYLATHAL	60	F	p	p	p					7.5	7.2	1,22,000
9	SELVARAJ	56	M			p					8.6	8.1	3,80,000
10	SUBRAMANI	60	M								8.6	7.9	2,16,000
11	NATARAJ	55	M		p						6.7	6.1	2,87,000
12	NAGARAJ	60	M								7.5	7.2	1,78,000
13	LEELAVATHI	67	F		p	p		p			8.1	7.4	2,09,000
14	KUPPAN	68	M					p			7.8	7.5	3,90,000
15	KUPPUSAMY	62	M			p		p			9	8.7	4,90,000
16	GOVINDRAJ	65	M			p					7.1	6	1,29,000
17	VIGNESHWARAN	68	M							p	8.8	7.3	1,67,000
18	SWAMINATHAN	75	M		p	p	p				8.5	7.6	2,78,000
19	LAKSHMI	77	F	p							6.7	6.4	1,90,000
20	VISWANATHAN	84	M	p							5.9	6.4	2,90,000

21	MUTHULAKSHMI	32	F		p	p			p		8.1	7.3	1,78,000
22	DURAISAMY	36	M				p				7.3	6.9	1,90,000
23	SARAVANAN	45	M			p	p				9	7.9	3,90,000
24	DHANALAKSHMI	48	F							p	5.9	6.9	4,89,000
25	SIVAKUMAR	56	M			p	p				8.4	8.1	5,18,000
26	TAMILSELVAN	53	M	p		p	p				6.7	6.4	2,01,000
27	RAJAMMAL	55	F		p	p					7.5	7.1	4,90,000
28	RANGAN	52	M	p		p		p			8.4	7	1,89,000
29	KANAGARAJ	56	M			p					8.5	8.2	1,90,000
30	MUTHUKUMAR	51	M								6.3	5.9	5,08,000
31	MAYILSAMY	57	M		p						7.6	7.1	2,90,000
32	KARTHIKEYAN	64	M				p	p			8.6	8.2	2,90,000
33	RAVEENDRAN	66	M	p				p			6.5	5.9	4,89,000
34	PALANIYAMMAL	67	F		p	p					8.5	7.8	4,38,000
35	RAVI	61	M			p					6	5.8	1,45,000
36	VENKATACHALAM	66	M			p					7.7	7.1	3,90,000
37	SHANTHI	70	F								8.7	8	4,90,000
38	SUBBULAKSHMI	72	F	p					p		8.6	8.1	5,00,000
39	SHANMUGAM	79	M				p				8.2	8.2	1,98,000
40	NAGESH	34	M		p	p		p			7.2	6.6	1,96,000
41	STALIN	38	M	p							7.5	6.9	2,90,000
42	ANGAPPAN	45	M		p	p	p				8.7	7.9	4,89,000
43	KANNAMAL	50	F								6.5	6.7	3,90,000

44	KUMARAN	55	M			p	p				8	7.9	4,00,000
45	ANGAMUTHU	52	M	p	p	p		p			7.7	7.3	3,08,000
46	SAVITHRI	58	F	p		p					8.1	7.9	4,09,000
47	SIVAN	52	M	p		p		p			8.5	8.1	3,89,000
48	RAJESH	58	M			p					6.1	5.8	4,08,000
49	SELVAN	52	M								7.5	6.9	5,00,000
50	FRANCIS	58	M	p	p						8.5	8.1	3,45,000
51	RAMKUMAR	64	M	p			p				8.5	8.2	1,35,000
52	CHANDRASEKAR	69	M		p		p				6.7	6	1,79,000
53	MANOKARAN	65	M	p				p	p		8.5	6	1,32,000
54	PRABHAHARAN	61	M		p	p					8.5	8.1	4,09,000
55	ARUMUGAM	67	M		p	p					7.5	8	2,09,000
56	RAMANI	75	F			p					9	8	3,90,000
57	THANGARAJ	76	M		p	p	p				7.1	6.7	2,99,000
58	SITHALAKSHMI	78	F								8.3	8	4,00,000
59	ANBUSELVI	37	F		p						7.3	6.7	2,88,000
60	SELVI	42	F		p	p					8.2	7.7	1,67,000
61	FATHIMA	46	F	p		p					8.3	8.2	2,67,000
62	SHEKAR	45	M		p	p	p	p			8.5	7.9	3,09,000
63	VISWAMBHARAN	52	M		p	p	p	p			7.3	7	4,78,000
64	PERIYASAMY	52	M	p	p	p	p				8.3	7.8	1,90,000
65	MARIYAPPAN	59	M	p		p	p	p			8.3	8	2,38,000
66	RAMESH	55	M	p		p		p			7.2	6.7	4,00,000

67	KARIYAN	58	M		p				p		7.7	6.4	2,05,000
68	MURUGAN	55	M								8.3	7.9	3,98,000
69	KARUPPUSAMY	59	M		p						8.5	8.1	1,56,000
70	SELVARAJ	66	M	p	p		p				7.5	7.3	2,78,000
71	SIVASHANKAR	68	M	p			p	p			7.5	7.1	2,88,000
72	KRISHNA	64	M		p			p			8.2	6.2	4,99,000
73	SURESH	63	M			p					8.3	7.5	4,90,000
74	SATHEESH	68	M		p	p			p		8	7.6	1,88,000
75	CHITRA	77	F			p					8.2	7.6	1,97,000
76	PANDISWARI	77	F								7	6.2	3,09,000
77	VELDURAI	80	M					p			7	6.6	4,80,000
78	KANDASAMY	39	M		p	p	p		p		7.1	6.8	3,90,000
79	RAMALAKSHMI	43	F		p	p					8.3	7.6	3,88,000
80	JAYA	48	F		p						8.5	8	1,90,000
81	BHASKAR	46	M			p	p	p			8.5	7.7	3,09,000
82	SUDALAIMANI	53	M		p	p		p			7.7	6.6	1,98,000
83	ABRAHAM	52	M	p		p		p			8.5	8	1,00,000
84	KANNAN	55	M	p		p	p				7	6.6	2,09,000
85	SELVARAJ	53	M			p		p			7.5	7.3	1,98,000
86	MARIMUTHU	58	M								7.5	6.8	1,00,000
87	MURUGESH	54	M								8.5	8.9	3,04,000
88	DEVAKI	59	F	p							5.9	6.2	2,22,000
89	GOWTHAM	66	M	p				p			8.5	8.3	1,30,000

90	RAJASEKARAN	68	M					p	p		8.1	7.4	2,90,000
91	SUDHA	63	F			p					8.3	8	4,00,000
92	KARUNAN	62	M			p					9	8	1,90,000
93	DHARMAN	67	M		p	p					9	7.9	2,99,000
94	RUKMINI	71	F	p				p			9	8.1	4,09,000
95	SAKUNTHALA	78	F	p							7.5	7	4,87,000
96	SAVITHRI	82	F			p					6.2	5.8	1,09,000
97	MUNIYANDI	29	M								7.5	6.9	2,07,000
98	DINESH	26	M								7.7	7.1	3,09,000
99	MURUGANANTHAN	23	M					p			7.6	7	1,40,000
100	VELUSAMY	27	M	p							8	7.2	3,50,000

KEY TO MASTER CHART

p	Presence of risk factors
age	Age in years
M	male
F	female
DM	Diabetes mellitus
HTN	hypertension
CAD	Coronary artery disease
PLT	Platelet count
MPV	Mean platelet volume
D	Dyslipidemia
S	Smoking
A	Alcoholism